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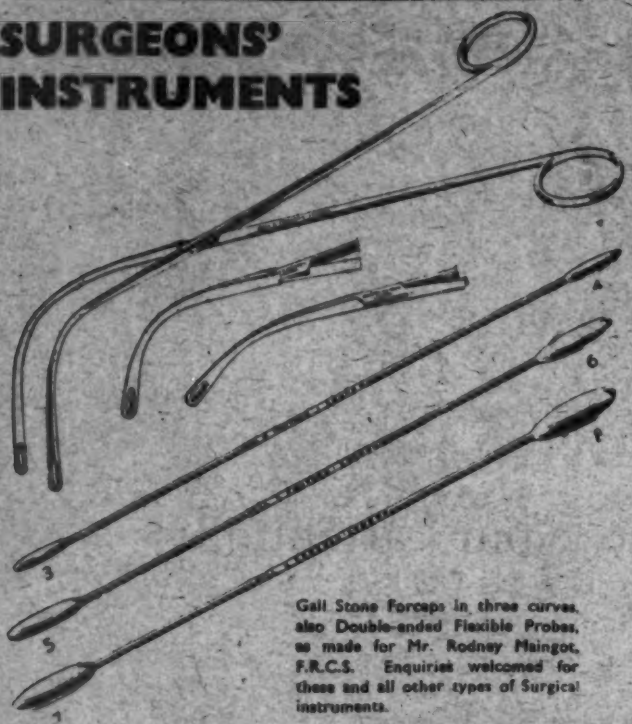

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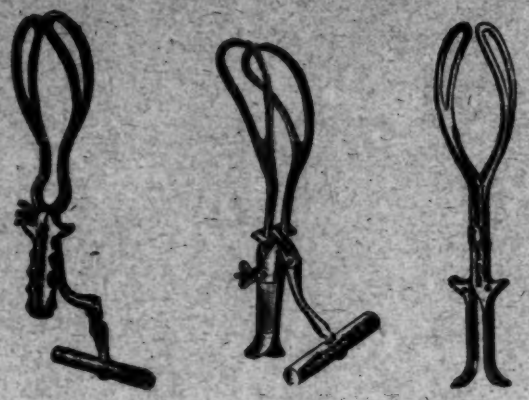

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BRITISH MEDICAL JOURNAL

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EFFECT OF A.C.T.H. AND CORTISONE THERAPY IN BLOOD DISORDERS

BY

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Recently a panel appointed by the Medical Research Council (1952) has given a summary of the responses to A.C.T.H. and cortisone in 88 patients suffering from various blood disorders. The present paper reports in more detail the results of this form of therapy in 24 patients, many of whom were included in the M.R.C. report. The literature on this subject is not yet extensive and is dealt with by Wintrobe *et al.* (1951). The mechanism of action of these hormones is uncertain, and will not be discussed here.

The cases are considered under three headings: (*a*) patients with purpura, (*b*) those with haemolytic anaemia, and (*c*) those suffering from miscellaneous blood disorders. Where no clinical or haematological response occurred, the results of treatment are given only in tabular form.

Purpura

Fourteen cases of purpura have been treated with A.C.T.H. and/or cortisone, and of these 10 had thrombocytopenic purpura. The condition appeared to be idiopathic in all but two.

In addition there were four patients suffering from persistent non-thrombocytopenic purpura in whom the exciting factor was unknown. These cases have been grouped together under the heading of "idiopathic non-thrombocytopenic purpura" (possibly allergic).

There was some evidence of a response to hormone therapy in the following six patients with thrombocytopenic purpura.

Case 1

This patient, a man aged 55 with no previous history of bleeding, woke up one morning to find his mouth full of blood; this was due to bleeding gums, and continued up to the time of admission three weeks later. He also developed petechiae on the limbs and trunk, and bruised easily; these features, too, were limited to the three weeks before admission. There was no history of the taking of drugs, or of infection, or of exposure to chemicals.

Apart from petechiae, bruises, and bleeding gums, the only abnormality found on admission was that the spleen was palpable on deep respiration. The haemoglobin level was 13.3 g.%, platelets 40,000 per c.mm., bleeding-time 29 minutes. The bone marrow contained numerous megakaryocytes and was otherwise normal. A diagnosis of idiopathic thrombocytopenic purpura was made. The patient was transfused with a pint (570 ml.) of blood on the third day in hospital and again on the sixth and ninth days. There was no clinical or haematological improvement. On the thirteenth day treatment with A.C.T.H. was begun, 25 mg. being injected six-hourly for eight days. Within 24 hours bleeding from the gums ceased and no further petechiae appeared. After eight days of treatment with A.C.T.H., however, there was no improvement in the haematological findings, the haemoglobin level being 10.6 g.%, platelets 30,000 per c.mm., bleeding-time 29 minutes. A month after cessation of A.C.T.H. therapy the platelet count was 50,000 per c.mm. and the bleeding-time seven minutes, but when the patient was next seen, 45 days after treatment was discontinued, the platelet count had risen to 254,000 per c.mm. and the bleeding-time was two minutes. During a follow-up period of a year there has been no further clinical evidence of a bleeding disorder, and a normal blood count and blood picture have been maintained.

Summary.—This was a case of idiopathic thrombocytopenic purpura in which it seemed likely that blood transfusion produced no improvement. Treatment with A.C.T.H. for a period of eight days in a dosage of 100 mg. daily coincided with clinical recovery. No immediate improvement in the platelet count occurred, but the blood figures returned to normal 45 days after treatment was stopped.

Case 2

A man aged 33, who had no previous history of a bleeding tendency or of exposure to infections, drugs, or chemicals, woke with blood in the mouth and found petechial spots on the tongue on the day before admission. By evening petechiae had developed all over the body, and at the time of admission he had haemorrhagic bullae in addition. His haemoglobin was 16 g.%, platelets 40,000 per c.mm., and the bleeding-time more than 30 minutes. He was given transfusions of a pint (570 ml.) of fresh blood on the first, second, and third days in hospital, but there was no improvement, and very gross haematuria developed. On the second day he was also given 200 mg. of cortisone by mouth in divided doses, and thereafter he had 100 mg. daily for six days, the dose then being progressively reduced for a further four days and supplemented by small doses of A.C.T.H. by injection. On the third day of treatment with cortisone there was marked clinical improvement. Bleeding from the mouth and urinary tract ceased and no further petechiae

developed. The platelets, however, were now only 20,000 per c.mm. and the bleeding-time was more than 20 minutes. Two days later the platelets began to increase significantly and the bleeding-time fell to two minutes. By the seventh day of cortisone treatment the platelet count reached 295,000 per c.mm. No clinical or haematological relapse has occurred during the eight months since treatment with cortisone ceased.

Summary.—This patient with idiopathic thrombocytopenic purpura showed no immediate improvement to blood transfusion, but a dramatic clinical and haematological improvement occurred during the administration of cortisone for seven days; this has persisted for eight months.

Case 3

A single woman aged 20, with no previous history of a bleeding disorder, had an irritation of the skin seven weeks before admission which developed into a severe exfoliative dermatitis. The cause was unknown, although it was suspected that it might have been due to the taking of headache powders. While under treatment for this dermatitis and after she had been in hospital for one month and was improving, petechiae developed all over the body, and haematuria, melaena, and epistaxis occurred. She had received codeine, diphenhydramine hydrochloride ("benadryl") (for one day only, as it caused swelling of the face and neck), "sulphatriad," and various local applications for the skin irritation and dermatitis, but whether any of these drugs were responsible for the bleeding tendency is unknown.

At this stage she was transferred to our medical ward, and blood examination showed the following figures: haemoglobin, 6.9 g.%; red cells, 2,500,000 per c.mm.; white cells, 10,600 per c.mm.; platelets, 25,000 per c.mm.; bleeding-time more than 40 minutes. Capillary resistance was very low. A diagnosis of thrombocytopenic purpura was made, but the causative factor was uncertain.

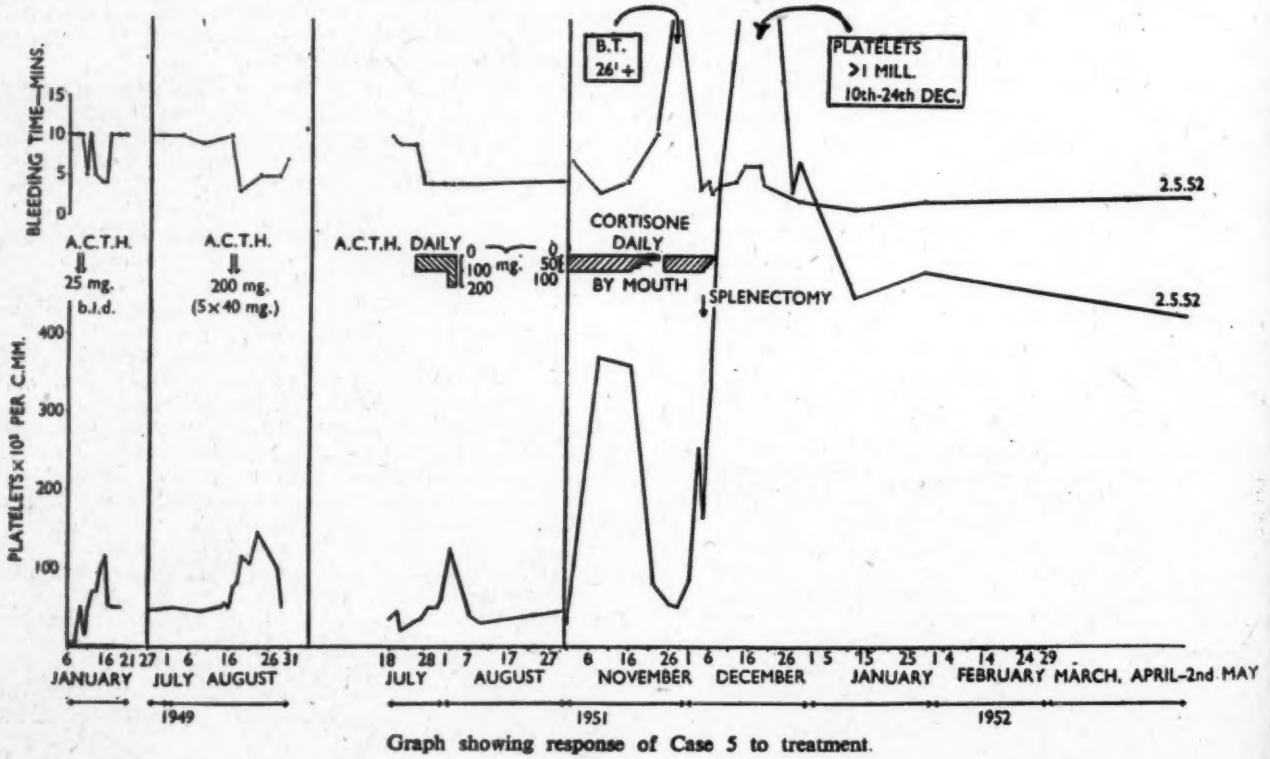
Treatment with A.C.T.H. was begun in a dosage of 25 mg. six-hourly by injection. A total of 1.7 g. was given, but it was necessary to transfuse 2 pints (1.1 litres) of blood on the second day of treatment and again three days later, as the patient was exceedingly ill. There was much less bleeding immediately after the first blood transfusion, and there was a distinct improvement after the fifth day of treatment, the petechiae disappearing and the external bleeding, including the haematuria, ceasing. The patient's general condition also improved, and the dermatitis became less severe. There was no immediate haematological response, the blood counts at the end of the A.C.T.H. therapy being: haemoglobin, 8.3 g.%; platelets, 20,000 per c.mm.; bleeding-time 20 minutes. Eight days later, however, the platelet count rose to 180,000 per c.mm. and the bleeding-time was 12 minutes. A further rise in the platelet count to 300,000 per c.mm. occurred, and the bleeding-time fell to three minutes. During a follow-up period of nine months there was no clinical or haematological relapse.

Summary.—This case of thrombocytopenic purpura was associated with exfoliative dermatitis of uncertain cause. Clinical and haematological "cure" followed treatment with A.C.T.H. and blood transfusion, and this "cure" was sustained for nine months.

Case 4

This patient, a woman aged 30, had a history of menorrhagia, petechiae, and bruising since the age of 15. A diagnosis of idiopathic thrombocytopenic purpura was made in 1947, and splenectomy was performed in August of that year. Unfortunately there was neither clinical nor haematological improvement from the operation. In May, 1951, the blood findings were: haemoglobin, 11 g.%; platelets, 45,000 per c.mm.; bleeding-time 14 minutes. A course of 25 mg. of A.C.T.H. was given six-hourly for 10 days by injection, but as there was no response this was followed immediately by the injection of 300 mg. of cortisone on the eleventh day, followed by 200 mg. on the twelfth day, in divided doses. The patient became psychotic, and the treatment had to be discontinued. The platelet count remained at 45,000 per c.mm., bleeding time 16 minutes. The bleeding tendency persisted.

Eight months later the patient was again given cortisone, this time by mouth, 50 mg. being administered six-hourly for 24 hours, and thereafter 25 mg. six-hourly for 13 days. Seven days after the treatment began the platelets rose from 30,000 to 155,000 per c.mm., and the bleeding-time fell from 48 to 5 minutes. This was the first haematological improvement that we had noticed during the five years she had been



Graph showing response of Case 5 to treatment.

under our care. Unfortunately, even during the time of treatment the platelets fell to 80,000 per c.mm. despite the continuation of cortisone therapy, which was discontinued because of the development of generalized oedema. There was no clinical or haematological improvement in the next two months.

Summary.—A patient with idiopathic thrombocytopenic purpura who did not respond to splenectomy. No response to treatment with A.C.T.H. occurred, but there was a temporary response to the oral administration of cortisone.

Case 5

A married woman aged 40 had a five-years history of episodes of bruising and petechiae, due to idiopathic thrombocytopenic purpura. Her initial haematological response to small doses of A.C.T.H. on two occasions has already been published (Robson and Duthie, 1950), and is shown in the Graph. The benefit from this treatment was only temporary; purpura recurred and menstruation became excessive. The patient was admitted to our wards in the Royal Infirmary of Edinburgh in July, 1951, the blood figures on that date being: haemoglobin, 11.7 g.%; platelets, 35,000 per c.mm.; bleeding-time, 10 minutes. She was treated by injections of A.C.T.H. in a dosage of 100 mg. daily for eight days, followed by 200 mg. on each of the next two days. There was a clinical remission on the fifth day of treatment, and on the last day the platelet count was 125,000 per c.mm. and the bleeding-time four minutes. This remission was, however, only very temporary, the platelet count falling to 40,000 per c.mm. five days after the cessation of treatment, although the bleeding-time was not increased. A month after the cessation of A.C.T.H. therapy petechiae were again seen.

In November, 1951, it was decided to try the effect of treatment with cortisone by mouth, and this was given in a dosage of 100 mg. daily for nine days, followed by a progressive reduction of dosage for six days. As will be seen in the Graph, this resulted in a rise of the platelet count from 30,000 to 370,000 per c.mm. on the ninth day of treatment, the bleeding-time falling from 7 to 3½ minutes. The platelet count began to fall, however, during the period of reduction of dosage, and was 80,000 on the last day, when only 25 mg. was taken. The bleeding-time had risen to 11 minutes. Two days later there was a recurrence of petechiae and bruising.

A further course of oral cortisone therapy again resulted in a clinical and a haematological remission, as shown in the Graph, the platelets rising from 50,000 to 250,000. The spleen was removed during this period of improvement. The platelets thereafter rose from 255,000 to 1,000,000 per c.mm., and then fell to 448,000 per c.mm. During a follow-up period of seven months there has been no clinical or haematological deterioration.

Summary.—This case of idiopathic thrombocytopenic purpura responded on three occasions to A.C.T.H. by injection, and later showed a better haematological response on two occasions to the oral administration of cortisone in a daily dosage similar to that of A.C.T.H.

Case 6

A married woman aged 32 had developed petechiae and bruising three years previously during the puerperium following her fourth pregnancy. At that time her platelet count was 50,000, and it had remained about that level ever since. While splenectomy was being contemplated, she became pregnant again for the fifth time. The pregnancy itself was uneventful, but she gave birth to a purpuric and thrombocytopenic son in November, 1950. This case has already been published by Robson and Walker (1951). The mother maintained comparatively good health after this, apart from occasional bruising, until June, 1952, when massive spontaneous bruising appeared on her legs. There were also a few petechiae, but no other evidence of bleeding. Blood examination showed a haemoglobin at 12.7 g.%; the platelets numbered 65,000, and the bleeding-time was 11 minutes.

TABLE I.—*Cases of Purpura not Responding to A.C.T.H. or Cortisone*

Case	Sex and Age (Years)	Spleen Removed	Before Treatment: Hb (g.%)	Platelets (per c.mm.)	Bleeding-time (Minutes)	Clinical Features	After Treatment: Hb (g.%)	Platelets (per c.mm.)	Bleeding-time (Minutes)	Clinical Features	Treatment	Days
						Idiopathic Thrombocytopenic Purpura						
A	F 22	Yes	6·0	30,000	8–20	Epistaxis; petechiae; bleeding gums	5·3	40,000	30+	Bleeding gums	A.C.T.H. 25 mg. i.m. 6-hourly	1–7
B*	F 29	No	(1)14·7	60,000	7–30	Bleeding gums; petechiae	12·8	55,000	8	Bleeding gums	A.C.T.H. 25 mg. i.m. 6-hourly	1–10
		‡No	(2)12·0	80,000	2½–23	Bruises	12·0	40,000	7–25	Petechiae	Cortisone by mouth 100 mg. daily	1–15
											Diminishing dosage	16–22
C†	F 58	No	11·2	40,000	20	Bruises; epistaxis; purpura; melaena	10·0	40,000	7	Bruises; purpura	A.C.T.H. 25 mg. i.m. 6-hourly	1–10
D*	F 5	,,	13·0	65,000	6	Bruises; purpura	13·6	65,000	6	Bruises; purpura	Cortisone orally 100 mg.	1
											50 ,,	2–9
											75 ,,	10–19
						Non-thrombocytopenic Purpura						
E	F 9	,,	11·4	260,000	15	Purpura; haematuria; oedema	11·4	Normal	—	Haematuria; oedema	Cortisone orally 50 mg.	1–5
											25 ,,	6–8
											10 ,,	9
F	M 43	,,	15·0	304,000	2	Purpura	15·0	365,000	3	Purpura	Cortisone orally 200 mg.	1–11
											150 ,,	12
											50 ,,	13
											A.C.T.H. i.m. 50 mg.	13, 22
											75 ,,	14, 21
											100 ,,	15–20
G	M 48	,,	15·2	472,000	2½	Purpura; colic; melaena	15·2	450,000	3	Purpura	Cortisone 200 mg. i.m.	1
											100 ,, ,,	2–5
											100 ,, orally	6–16
											75 ,, ,,	17–28
H	F 37	,,	13·1	250,000	3½	Purpura; ecchymosis	13·0	220,000	2	Purpura; ecchymosis	Cortisone by mouth 200 mg.	1
											100 ,,	2–11
											50 ,,	12
											25 ,,	13

* Subsequently responded to splenectomy. † Purpura started 6 months after gold injections. ‡ Six months later.

Cortisone by mouth was given in a dosage of 200 mg. on the first day, followed by 100 mg. a day for eight days. During this period no further skin lesions developed; the platelet count rose to 145,000 on the seventh day of treatment, and the bleeding-time fell to 3½ minutes. Despite continuation of cortisone therapy in the same dosage the platelet count fell to 105,000 and the bleeding-time increased to eight minutes. Accordingly, the dose of cortisone was increased to 200 mg. for three days, but the platelet count did not rise again. Cortisone therapy was discontinued four days later, during which period the daily dosage was gradually reduced. During this time the platelet count fell to 20,000 and the bleeding-time rose to 10 minutes.

Summary.—This case of idiopathic thrombocytopenic purpura showed an initial temporary clinical and haematological improvement on cortisone by mouth. Haematological relapse occurred before cortisone therapy had been withdrawn.

Details of the eight cases of purpura in which hormone therapy was unsuccessful are shown in Table I.

Haemolytic Anaemia

In a previous paper (Davidson *et al.*,* 1951) an account was given of three cases of haemolytic anaemia treated with A.C.T.H. Since then we have used hormone therapy in treating two further patients.

Case 7

A man aged 56 had been dyspnoeic on exertion for 18 months. Increasing tiredness was associated with the dyspnoea, but pallor was not noticed until a week before his first admission to hospital. There was no history of blood loss or of jaundice. No member of his family had, to his knowledge, been anaemic or jaundiced. On examination he was seen to be pale and slightly icteric. The liver was just palpable on deep inspiration and the lower pole of the spleen reached to within 2 in. (5 cm.) of the umbilicus. The urine contained a great excess of urobilinogen, and the serum bilirubin was 4 mg. per 100 ml. The haemoglobin level was 8 g.%, but an accurate red-cell count was difficult because of clumping of the cells. A reticulocytosis of about 15% was repeatedly found. The marrow was normoblastic. The direct Coombs test was positive and cold agglutinins were present; there was increased red-cell fragility. A sudden fall in the haemoglobin level to 5 g.%, a rise in the reticulocyte count to 26%, and a deterioration in the patient's condition indicated an increase in the haemolytic process. Accordingly he was given 2 pints (1.1 litres) of packed cells, which raised the haemoglobin level to 7 g.%. The reticulocyte count, however, remained at 26%.

Thereafter treatment consisted of injection of A.C.T.H. in a dosage of 25 mg. six-hourly for 10 days. This treatment brought a great improvement in his strength and well-being, a rise in the haemoglobin level to 10 g.%, the red cells now numbering 3,300,000 per c.mm., and a fall in the reticulocyte count to 15% and in the serum bilirubin from 4 to 1.7 mg. per 100 ml. The urine now contained only a trace of urobilinogen. The Coombs test, however, remained positive and cold agglutinins were still present.

The patient was discharged from hospital, but owing to deterioration of his condition he had to be readmitted 30 days after the A.C.T.H. therapy had been discontinued. The haemoglobin level had fallen to 6.5 g.% and the red cells to 2,530,000 per c.mm., while the reticulocyte count remained between 20 and 35%.

Treatment on this occasion was with cortisone given by mouth to a total of 925 mg. in eight days. During this period his condition deteriorated and 2 pints (1.1 litres) of blood had to be transfused. The reticulocyte count remained high, and even with blood transfusion the haemoglobin level did not rise above 6.4 g.%. Treatment was changed to A.C.T.H. given parenterally in a dosage of 25 mg. six-hourly for nine days, then 25 mg. eight-hourly for seven days. The patient showed a distinct clinical and haematological improvement, the haemoglobin level rising to 10.2 g.% and the red cells to 3,330,000 per c.mm., and the reticulocytes falling to 9.2%. A.C.T.H. therapy was continued and the spleen was removed.

The daily dose of A.C.T.H. was then progressively reduced and hormone treatment was finally terminated nine days after operation. An immediate rise in the haemoglobin level and red cell count was noted after splenectomy; this was due to autotransfusion from manipulation of the spleen at operation. A large reduction in the haemolytic process occurred during the next 14 days. A further moderate recrudescence of haemolytic activity again developed, as indicated by a fall in the haemoglobin value and a rise in the reticulocyte count, together with an increase of urinary urobilinogen. Accordingly, A.C.T.H. was again given in divided doses, 1 g. being administered parenterally over 14 days. This resulted in a steady rise of haemoglobin level to 12.5 g.%, and the red cells to 4,020,000 per c.mm., with a fall in the reticulocytes to 2.8%. The patient felt very well. Three months after the cessation of hormone therapy, when he was seen as an out-patient, there was no clinical or haematological deterioration. Reticulocytes were now 1%. The Coombs test remained positive.

Summary.—A patient with idiopathic acquired haemolytic anaemia who improved temporarily with A.C.T.H. therapy but not with cortisone by mouth in a dosage of 100 mg. daily. A definite though delayed clinical and haematological improvement resulted from splenectomy supplemented with A.C.T.H.

Case 8

This patient was a woman aged 69 with rheumatoid arthritis and anaemia. As her case is of interest in relation to the arthritis, it will be published in more detail elsewhere. The anaemia was of a haemolytic type, with reticulocytes ranging from 9 to 18%. The urine contained an excess of urobilinogen. The direct Coombs test was positive, and there was evidence of cold agglutinins in the blood. When A.C.T.H. therapy was begun the haemoglobin level was 7.4 g.% and the red cells numbered 2,400,000 per c.mm. A.C.T.H. was given in divided doses by injection, to a total of 1.42 g. in 10 days. The haemoglobin level rose to 9.5 g.% and the red cells to 2,950,000 per c.mm., but fell slightly to 8.3 g.% and 2,750,000 respectively when the A.C.T.H. therapy was stopped. Cortisone was then given by mouth in a dosage of 100 mg. daily for three days and the counts returned to the highest level obtained with A.C.T.H. (9.5 g.% and 2,950,000 per c.mm.). The dosage of cortisone was now increased to 125 mg. daily for two days, followed by 175 mg. daily for four days and then 150 mg. daily for three days. The haemoglobin level rose to 13.3 g.% and the red cells to 3,900,000 per c.mm., the reticulocytes falling to normal levels. The Coombs test remained positive. A reduction in the dosage of cortisone resulted in an immediate fall in the level of the haemoglobin and red-cell counts.

Summary.—A case of acquired haemolytic anaemia in a patient with rheumatoid arthritis in which there was temporary benefit both with A.C.T.H. and with cortisone therapy.

Miscellaneous Group

The remaining patients consisted of four cases of aplastic anaemia, one of which was due to gold therapy, one case of myelosclerosis, two of acute leukaemia in adult patients, and one infant with eosinophilia associated with a grossly enlarged spleen. There was no clinical benefit in any of these patients, and, as will be seen from Table II, the blood picture was unchanged.

Discussion

In three cases of thrombocytopenic purpura of the present series there was a clinical and haematological "cure" following treatment with A.C.T.H. or cortisone supplemented by blood transfusion. The illness in all three

TABLE II.—*Miscellaneous Blood Disorders not Responding to A.C.T.H. or Cortisone*

Before Treatment

TABLE II.—*Miscellaneous Blood Disorders not Responding to A.C.T.H. or Cortisone*

Case	Diagnosis	Sex and Age	Before Treatment							After Treatment						Days
			Hb (g.%)	R.B.C. (mil. per c.mm.)	W.B.C. (per c.mm.)	Retics. (%)	Platelets (per c.mm.)	Other Findings	Marrow	Hb (g.%)	R.B.C. (mil. per c.mm.)	W.B.C. (per c.mm.)	Retics. (%)	Platelets (per c.mm.)	Other Findings	Treatment	
S	Aplastic anaemia (after gold therapy)	M 34	8·0	2·41	2,500	<1	30,000		Reactive	5·3	1·35	1,750	1	15,000		A.C.T.H. 25 mg. i.m. 6-hourly	1–10
T	Aplastic anaemia	F 49	6·3	1·85	1,700	<1	37,000		Aplastic	6·3	1·98	3,200	<1	60,000		Cortisone i.m. 300 mg. 200 ,, 100 ,,	1 2 3–13
U	Aplastic anaemia	M 61	3·7	1·13	2,200	4·2	—		Reactive	3·0	0·79	4,800	7·5	—		(2 pints blood transfused) Cortisone i.m. 300 mg. 200 ,, 100 ,,	1 2 3–13
V	Aplastic anaemia	F 51	9·6	2·58	2,400	<1	20,000		Aplastic	9·9	3·56	2,200	<1	20,000		(4 pints blood transfused) A.C.T.H. 25 mg. i.m. 6-hourly Cortisone by mouth 50 mg. 100 ,, 200 ,,	1–6 7–9 10–11 12–16
W	Acute myeloid leukaemia	F 32	7·3	2·81	24,000	<1	25,000	Blast cells, 32%	Chiefly myeloblasts and myelocytes	9·2	3·73	69,000	<1	25,000	Blast cells, 40%	(2 pints blood transfused) Cortisone by mouth 200 mg. 100 ,,	1 3–14
X	Acute lymphatic leukaemia	F 21	6·0	2·36	8,000	10	35,000		Lymphocytes and lymphoblasts	4·4	1·63	42,600	18·4	30,000		(7 pints blood transfused) A.C.T.H. 25 mg. i.m. 6-hourly	1–10
Y	Eosinophilic leukaemia	M 1	10·0	—	30,000	<1	—	Eosinophils, 53% Coombs test positive		10·0	—	25,000	—	—	Eosinophils, 38% Coombs test positive	Cortisone 20 mg. by mouth	1–9
Z	Myelosclerosis	M 26	(1) 6·3	2·2	1,900	<1	220,000		Some fibrous replacement	7·0	2·5	2,600	<1	195,000	Coombs test positive	A.C.T.H. 25 mg. i.m. 6-hourly Cortisone i.m. 100 mg. 200 ,, 50 ,,	1–14 1–2,5,6 3,4,7–10 11,12
			(2) 6·3	2·3	2,600	<1		Coombs test positive		6·6							

patients had been of short duration, and therefore it is not possible to be certain to what extent the hormone therapy was responsible for the improvement which occurred. Indeed, in one case the platelet rise did not occur until more than a month after A.C.T.H. therapy was terminated. A fourth patient, who had not responded to splenectomy for idiopathic thrombocytopenic purpura, showed no improvement with 100 mg. of A.C.T.H. daily for 10 days. She did, however, develop a temporary but significant increase of platelets from the administration of 800 mg. of cortisone by mouth over a period of seven days. A fifth case—a woman with idiopathic thrombocytopenic purpura—repeatedly responded to small courses of A.C.T.H. by injection, but when cortisone was given by mouth in the same dosage as the preceding course of A.C.T.H. the platelet response was much higher. It was noted in this same patient that withdrawal of cortisone led to an increase of the bleeding-time over its previous level. A sixth case showed a significant but temporary response to cortisone by mouth.

The remaining four patients with idiopathic thrombocytopenic purpura, and four with non-thrombocytopenic purpura, apparently of an allergic type, did not respond to hormone therapy. One of the latter group, however, who suffered from Henoch's purpura, was quite certain that his abdominal colic was rapidly relieved by cortisone although the purpura was unchecked. This patient, who was a doctor, was satisfied that muscular weakness was felt during cortisone therapy if he did not take the potassium citrate that had been prescribed.

There seem to be no satisfactory clinical or haematological criteria which would enable an accurate forecast to be made whether any particular case of thrombocytopenic purpura will or will not respond to hormone therapy. It is, however, clear that a failure to respond to such treatment does not indicate that splenectomy will not be successful (see Cases B and D, Table I). Moreover, as already mentioned, a case of thrombocytopenic purpura which has failed to respond to splenectomy can show a response to cortisone (Case 4).

In two patients with acquired haemolytic anaemia there was a response to A.C.T.H. or cortisone, but this improvement was transient.

No beneficial results were obtained in a small group of patients suffering from aplastic anaemia, acute leukaemia, or myelosclerosis.

Summary

A.C.T.H. or cortisone was administered to 14 cases of purpura, to 2 cases of idiopathic acquired haemolytic anaemia, and to a small group of patients suffering from aplastic anaemia, leukaemia, or myelosclerosis.

Three cases of thrombocytopenic purpura of short duration were apparently cured by hormone therapy.

Temporary beneficial effects were produced in three cases of idiopathic thrombocytopenic purpura and two cases of idiopathic acquired haemolytic anaemia. Such remissions may be of value in allowing splenectomy to be undertaken with greater safety.

No beneficial results were obtained in the remaining eight cases of purpura and in a small number of patients suffering from a diverse group of blood disorders.

The cortisone and A.C.T.H. used in this investigation were supplied by the Medical Research Council. We would express our gratitude to Dr. A. R. Gilchrist and Dr. J. J. R. Duthie for permission to treat the two patients with haemolytic anaemia.

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TRACHEOTOMY IN ACUTE OBLITERATIVE LARYNGOTRACHEO-BRONCHITIS

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This condition was first commented on by Gover (1918) and Lynah (1919) during the influenza pandemic, and the term acute laryngotracheobronchitis was used subsequently by Baum (1924). A detailed review and bibliography of the condition is given by Neffson (1949). Unfortunately the precise significance of the term is not always clear. Brighton (1940) believed it should include only cases requiring tracheotomy or other instrumental relief. Morgan and Wishart (1947), however, considered that it should apply to all cases of "spasmodic croup." Although the condition is usually regarded as an acute non-diphtheritic respiratory infection, Gittins (1942) also included allergy and trauma as aetiological factors.

Because certain parts of the respiratory tract are more often affected than others, some workers have attempted a further subclassification to emphasize this. Neffson (1949) stressed the importance of infraglottic and supraglottic types; Gittins (1942) also subdivides his classification in relation to the main site of the lesion; and Forfar, Keay, and Thomson (1951) have reserved the term for cases of acute laryngotracheitis which have auscultatory signs of bronchitis.

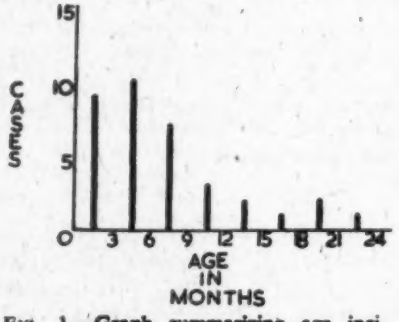

FIG. 1.—Graph summarizing age incidence.

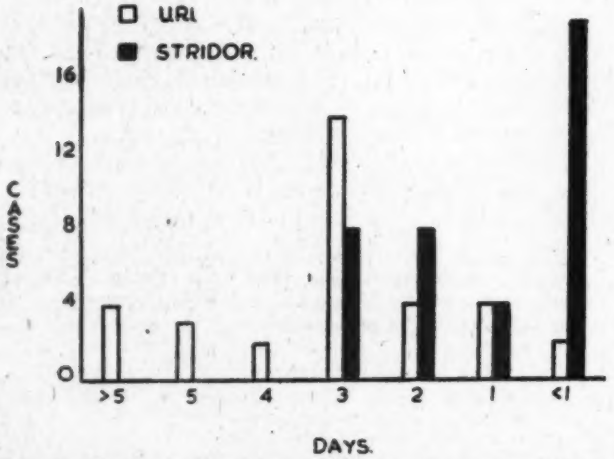

FIG. 2.—Graph showing time incidence of upper respiratory infection and stridor in relation to admission.

The term acute obliterative laryngotracheobronchitis is applied in the present series of 39 cases to an acute non-diphtheritic respiratory infection which occurred in young children and caused respiratory embarrassment due to obstruction of the respiratory passages. In 37 cases the main emphasis of the lesion was an obstruction of the small bronchi and terminal bronchioles.

A fairly characteristic clinical pattern was present in most cases. There was a history of an upper respiratory infection for three days, and usually stridor did not appear until the day of admission. The occurrence of stridor was the main reason why the parents consulted their family doctor or brought the child to hospital. On admission the child was usually restless and pale, with noticeable inspiratory and expiratory stridor. The respiratory rate was raised, intercostal recession was present, and in some cases suprasternal indrawing was also to be seen. In some of the more acutely ill children cyanosis was present, and was always a serious sign. Localizing signs in the chest were uncommon, and generalized rhonchi were the most frequent auscultatory finding. The heart rate was always rapid, often considerably so. Severe inflammation of the throat was not a frequent finding. The chest was on *x*-ray examination normal or showed slight emphysema. The white cell count was more often normal than raised, while throat swabs did not grow a specific organism. After admission and treatment the patients usually lost their stridor between the third and fifth day, and were fit for discharge after a further period of five days.

The physical findings were as follows. Stridor occurred in all 39 cases, rhonchi in 23, restlessness in 23, pallor in 20, and cyanosis in 12. There were two cases of pneumonia. The age incidence, and the time incidence of upper respiratory infection and stridor in relation to admission, are shown in Figs. 1 and 2 respectively.

Medical Treatment

The basis of treatment used in all cases of this series was atmospheric humidification, which was produced by steam-kettle and tent, or aerosol vaporizer. In the more severely affected patients oxygen therapy was combined with humidification. All the children were given antibiotics: terramycin was used in 15 and chloramphenicol in 10. In two of these cases terramycin was given intravenously, but otherwise the drugs were administered orally. Terramycin was given in a dose of 50–80 mg. per lb. of weight (110–175 mg./kg.), while chloramphenicol was used in doses of 100 mg. per lb. (220 mg./kg.). The remaining patients received a combination of drugs: six were given penicillin combined with chloramphenicol or terramycin, five had penicillin and streptomycin, while three received penicillin and aureomycin. In several cases the initial use of penicillin and streptomycin was because the young child was too ill to take adequate amounts of drugs by mouth.

Of these 39 cases 29 ran the characteristic course described above, and recovered with medical treatment. There was one "medical" death. Nine children, however, required tracheotomy; reports of three of these are presented to emphasize the particular indications for the operation.

Typical Cases for Tracheotomy

Case 1.—A boy aged 4½ years was admitted with a week's history of a cough and 12 hours' history of respiratory distress. On examination his temperature was 100.8° F. (38.2° C.), pulse 100, and respirations 32; there was cyanosis, and excess mucus in the mouth with diminished air entry in the chest and slight recession. Crystalline penicillin, 1 mega unit, was given immediately and pharyngo-laryngeal suction was carried out, using a direct-vision laryngoscope.

This caused deep cyanosis, and immediate tracheotomy was performed. Relief of obstruction was dramatic. Further treatment consisted of oxygen with aerosol mist, intravenous terramycin 1 g. in 24 hours, and then oral terramycin for one week. The child was well on the second day, the tracheotomy tube was removed on the fourth day, and he was discharged on the tenth day.

Case 2.—On the day of admission the child, a boy aged 18 months, developed a croupy cough and because of general deterioration was transferred to hospital. On admission he was cyanosed and dyspnoeic, and had slight costal recession. There were no localizing chest signs. Temperature 103° F. (39.4° C.), pulse 180. The child was under observation in oxygen for one hour. At the end of this period the recession and cyanosis had increased, so an elective tracheotomy was performed followed by bronchial suction. The latter produced a fair quantity of mucopus, more from the left than the right bronchus. This procedure caused immediate lessening of recession, and improvement in colour and in his general condition. One hour later the child's condition was satisfactory, and four hours later oral terramycin was begun, 250 mg. being given every six hours. Eight hours after operation bronchial suction was repeated because the respiratory signs were increasing. Casts of moderate and small size were removed from both sides, the improvement being dramatic. The child was then nursed in steam for 24 hours and afterwards in oxygen with aerosol mist. Two days after admission the child began to feed well and take an interest in his surroundings. Special nursing was discontinued on the fourth day, the tracheotomy tube was removed on the fifth day, and the child was discharged on the 13th day after admission.

Case 3.—A girl aged 1 month had a cold for five days before admission, with a cough for two days. On the day of admission she refused all feeds, and by 3 p.m. was having difficulty in breathing. Examination showed a slightly cyanosed pale baby with some chest recession. With oxygen therapy the colour improved and she was nursed overnight in an oxygen tent and received penicillin and streptomycin therapy. At 10 a.m. her condition was good, but by midday rib recession was recurring, and at 1.50 p.m. she had become pale and cyanosed, with definite basal recession. Tracheotomy and bronchial suction were performed, with marked improvement; the cervical venous distension and recession disappeared, although facial pallor persisted. Bronchial suction was done at three-hourly to four-hourly intervals, and by 10 p.m. respirations were regular, with minimal recession. Oral feeds were taken well next day, and the child was nursed in oxygen with aerosol. Convalescence was uneventful, the tracheotomy tube was removed on the sixth post-operative day, and she was discharged from hospital on the 18th day.

Comments on Cases 1-3.—In Case 1 immediate tracheotomy was life-saving, and the laryngeal region was the main site of inflammation. Case 2 was more typical of our series, and tracheotomy was done as an elective procedure one hour after admission. Case 3 had an elective tracheotomy 24 hours after admission because of deterioration following initial improvement.

FIG. 3.—Specimen of lung from a post-mortem case aged 3 months. The polythene tubes were passed and the lung dissected to show their position.

Operation

Tracheotomy was performed in all cases through a transverse skin incision and under local analgesia. Once through the deep fascia, dissection was limited to the midline, and a low tracheotomy was performed, the largest possible tube being inserted. The only difficulty was the presence of a large thymus in two of the smaller babies, necessitating downward retraction to expose the trachea.

Method of Suction.—At first we used water-pump suction, but very soon we realized that the negative pressure achieved was inadequate to remove the thick viscid secretions. We now use an electric sucker and polythene tubing (Fig. 3). The polythene tube was the largest that would pass through the outer tracheotomy tube. Rotation of the head combined with twisting of the curved tubing allowed easy passage of the tube into either main bronchus and down distally to a distance of 4–6 in. (10–15 cm.) in a child of 3 to 6 months (Fig. 3). The histological composition of the casts removed is described by Emery (1952).

Post-operative Care

Suction was repeated in most cases every three to four hours during the first post-operative day, and in one case for as long as three days. Bronchial lavage was attempted in one case to aid removal of viscid plugs, but the results were not impressive.

No serious complication resulted from this method of suction despite the frequency with which it was used, and it was performed by both junior and senior medical residents. The nursing staff were instructed in the use of a simple suction with a soft rubber catheter to keep the tracheotomy tube clear of mucus. No crusting of secretions was encountered.

Because of one fatality early in the series (Case 6) we continually stressed that it was important to have a special nurse, that the patient should not be hidden in a canvas tent, and that adequate night lighting should be available. When any sudden deterioration occurred the nurse was instructed to remove the inner tube immediately and apply suction to the outer tubing while another nurse called medical assistance.

Complications.—Surgical emphysema was seen in the tissues of the neck of one case on a routine check radiograph but was not demonstrable clinically. One other case had a persistent croup which disappeared within four weeks.

Fatal Cases

Of the nine patients who came to tracheotomy three died; these cases are described below, as is the one "medical" death.

Case 4.—A boy aged 7 weeks was admitted as an emergency with a temperature of 107° F. (41.7° C.) and cyanosis. The history was of snuffles and a dry cough for one week. Twelve hours before admission the child appeared feverish, and from that time refused all feeds. Six hours before admission he had a convulsion. On admission he was in extremis, with cyanosis, laryngeal stridor, and severe intercostal recession. The chest signs were of generalized basal crepitations with diminished air entry, and, apart from an abnormally shaped skull, other systems appeared normal. After emergency intubation the respiratory distress decreased but not the cyanosis. The child was then put into an oxygen tent and given 200,000 units of crystalline penicillin three-hourly and streptomycin 50 mg. six-hourly. Three-quarters to one hour later respiratory distress was so severe that intubation was repeated with light suction of tracheal secretions; again there was some improvement. Twenty minutes later the child's condition had deteriorated and he appeared moribund. An indwelling endotracheal tube was passed and suction repeated. Improvement on this occasion was minimal, and tracheotomy was at once performed. This produced three to four minutes of acapnoeic anoxia, and when seen half an hour later in oxygen the child was definitely easier but remained cyanosed. Bronchial suction was repeated twice in the next three hours, but the patient gradually deteriorated, and died four and half hours after tracheotomy.

Case 5.—A boy aged 4 months was admitted with a four-days history of cough and a five-hours history of respiratory distress and stridor. On examination he was restless, with marked general pallor and cyanosis of the lips and fingers. A loud stridor was audible and there was marked recession of his chest wall. Apart from generalized moist sounds physical examination of the chest was negative. Temperature 101° F. (38.3° C.), pulse 160. Crystalline penicillin, 200,000 units, was given three-hourly and the child put into an oxygen tent. The cyanosis disappeared in oxygen and the child seemed more restful. Two hours after admission the resident medical officer found the patient in extreme respiratory distress, with pallor, cyanosis, and restlessness. Tracheotomy was performed in the ward within 10 minutes and an attempt was made to aspirate the bronchi with water suction. This failed, and as the child's condition was rapidly deteriorating it was returned to the oxygen tent and artificial respiration given. Efforts to procure effective suction were unsuccessful and, despite resuscitative measures, the baby died half an hour after the operation.

Case 6.—A boy aged 2 months was admitted with a 48-hours history of cough, running nose, and wheezing. During the last 24 hours he had had four attacks of respiratory distress, and was sent in because of the last, which was more severe. On examination he was not unduly distressed; he was a good colour, but had a definite stridor. The only abnormal physical signs were occasional generalized rhonchi and tachycardia. Oral chloramphenicol was given six-hourly. Next day the chest signs were more severe and the child was placed in a steam tent. By 4 p.m. rib recession was pronounced, with cyanosis and extreme restlessness. Tracheotomy, with bronchial suction, was performed at 4.30 p.m. Following suction, which was quite productive, cyanosis decreased. Bronchial suction was repeated twice before midnight, and the child was nursed in steam. At 2 a.m. his condition had become much worse, further suction was performed and oxygen administered. Artificial respiration was performed in the oxygen tent for a period and aerosol therapy begun. Suction was repeated on two or more occasions, and by 10 a.m. the child was sufficiently improved to take a feed. Progress throughout the day was satisfactory, but quite suddenly at 6 p.m. the child became acutely distressed and died.

Case 7.—This patient, a boy aged 7 months, was admitted with a history of an upper respiratory infection for three days and stridor on the day of admission. He was treated in a steam tent and given penicillin, 100,000 units six-hourly, and streptomycin, 20 mg. per lb. (44 mg./kg.) of body weight. Six hours after admission he was more distressed, and had considerable recession. Cyanosis appeared, and he died from apparent suffocation.

Comments on Cases 4–7.—From the onset Case 4 was most unfavourable, but there is no doubt that the repeated intubation with suction failed to produce adequate clearance of the air passages and merely added laryngeal obstruction to the child's difficulties. In Case 5, mismanagement is seen in that the initial clinical picture with cyanosis did not prompt more vigorous treatment. The tracheotomy was left until the child was in extremis, and electrical suction was not available. Case 6 died shortly after the routine changing of the inner tracheotomy tube, and when one of us (J. N. B.) reached the dead baby this tube was found to be completely blocked with inspissated mucus. Death was due to asphyxia, although clinically the child was making a satisfactory recovery before this. The deterioration in Case 7 might have been stopped had an elective tracheotomy been done. Death appeared to be due to suffocation.

Relevant Extracts from P.M. Reports

Naked-eye Appearance of Lung from Case 4.—The trachea contained brownish-grey tenacious material. Similar material extended into the orifices of the largest bronchi and a pale thread could be seen extending down almost all of them. The lung showed some areas of collapse, with small pleural petechiae. No areas of consolidation were seen.

Lung Histology, Case 5.—Areas of collapse and abnormally distended lung were present with patches of early bronchopneumonia. There was a purulent infiltration of small bronchi and some intra-alveolar oedema. In some bronchi a cellular membrane was adherent to the mucosa.

Naked-eye Appearance of Lung from Case 6.—The bronchi contained yellowish mucus, and this appeared to become tenacious as the smaller bronchi were opened. No obvious areas of consolidation were seen, and on slicing the lung some of the small bronchioles seemed to be completely blocked with pale mucoid material. *Lung histology:* areas of alveolar oedema, dilatation and collapse were present, and some bronchi showed destruction of the epithelium and obliteration of the lumen.

In Case 7 no necropsy was performed.

Discussion

Almost all workers are agreed on the value of atmospheric humidification, which may be brought about by steam-kettle or aerosol vaporizer, and to this therapy oxygen can be added with definite advantage. The value of wetting agents is still under investigation (Gorman, 1950; Hall, 1952).

A precise statistical analysis of the value of any single antibiotic in these cases was not possible, but on the basis of clinical improvement no single antibiotic was specific. There can be no doubt, however, that antibiotics having a wide antibacterial range are of the greatest value in preventing secondary bacterial infection, which was previously such a serious complication. Preparations which can be given intramuscularly or intravenously have an added advantage, as often the child may be too ill to take medicines orally. With the use of these methods most of the patients should recover, and in our series 29 cases responded rapidly. Opinion is divided on the value of tracheotomy. Baum (1945) believed that concentrated plasma, given intravenously in doses of 25–40 ml., relieved the obstructive symptoms. While he admitted that some cases might require tracheotomy, he felt that the use of concentrated plasma and bronchoscopic suction would save many cases from operation. Forfar, Keay, and Thomson (1951) were not impressed with the value of tracheotomy in two of their 22 cases, as both of those operated upon died. McEntee (1949) stated that delay would avoid some tracheotomies and would prevent some deaths, but he offered no figures to support his view. Neffson (1949) felt that the main use of tracheotomy was in treatment of cases with supraglottic oedema. However, in a review of 549 children who had suffered from acute laryngotracheobronchitis, Morgan and Wishart (1947) stated that tracheotomy was the operation of choice, and that it should be performed early in the disease. In a study of 70 patients, 11 of whom were operated upon, von Leden (1951) also concluded that early tracheotomy is of great value. His operative mortality was *nil*. Braestrup (1949) is convinced that early tracheotomy in severe cases of acute obliterative laryngotracheobronchitis is one of the most important points in the management of these patients.

The condition seen by us was one of obstruction of the smaller bronchi by viscid secretions which occurred early in the disease. The degree of anoxia varied according to the extent of this obstruction. If this was severe early death was likely to be due to mechanical obstruction rather than toxaemia. Removal of this obstruction can readily be achieved by adequate and, if necessary, repeated suction.

The possible ways in which suction may be applied are through an endotracheal tube, by bronchoscopy, or by tracheotomy. Repeated suction through an endotracheal tube may do more harm than good even when performed by a skilled operator, as in one of the fatal cases of this series (Case 4). For this reason we feel that intubation

or bronchoscopy should be limited to an emergency procedure prior to tracheotomy. In these cases further emphasis must be placed on repeated suction. The performance of a tracheotomy, and then suction using polythene tubing, ensures that the smaller bronchi may be reached and cleared.

When necessary, the decision should be to do the tracheotomy as an elective procedure, and the exact time interval before the operation must vary with each individual case. This may range from immediately on admission up to 36 hours later. The use of tracheotomy as a last desperate expedient can only bring its performance in acute obliterative laryngotracheobronchitis into disrepute.

Summary and Conclusions

Thirty-nine cases of acute obliterative laryngotracheobronchitis are described. Their clinical course and medical treatment are given and their management is discussed, with especial reference to the use of tracheotomy.

The indications for elective tracheotomy are : (1) the appearance of cyanosis ; (2) extreme fatigue ; (3) increasing restlessness, pallor, and stridor, with an associated diminution of air entry.

Our cases fall into three groups. (1) *Immediate emergency tracheotomy* (*see Case* 1), which is necessary where there is acute glottic obstruction. (2) *Early elective tracheotomy* (*see Case* 2) : these are the patients who rapidly deteriorate despite adequate medical treatment. They should be under observation for a period of one hour and then have tracheotomy performed. (3) *Late elective tracheotomy* (*see Case* 3): these patients at first respond to medical treatment, but later their condition deteriorates. When this occurs they should be observed for a period of one hour and then have tracheotomy performed. These cases usually do not present until 24–36 hours after admission.

We wish to thank Dr. T. Colver, Professor R. S. Illingworth, and Mr. R. B. Zachary for access to their cases; and Professor E. J. Wayne for advice and criticism in preparation of this paper.

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A branch of the Davidson Clinic for the out-patient treatment of psychoneurotic illness and emotional disorders was opened last month in Glasgow by the Lord Provost. The original Davidson Family Clinic (named after the Davidson Church in whose vestry the clinic was first housed) was established in Edinburgh in 1941. The Clinic is open to anyone with psychoneurotic illness, fees being charged according to the patient's means. Treatment is by psychoanalysis, with special emphasis on the correction of family disharmonies. The Edinburgh Clinic has a staff of 12 analysts, 6 of whom are medically qualified. It is the policy to use carefully selected lay therapists working under the supervision of the medical staff, so as to increase the turnover of patients. The Clinic is a registered charity and appeals to the public for funds. No grants have so far been allocated to it from National Health Service or local authority funds.

ACUTE LARYNGOTRACHEOBRONCHITIS IN CHILDREN

A STUDY OF THE INCIDENCE AND PATHOLOGY

BY

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[WITH SPECIAL PLATE]

The impetus given to the investigation of croup by Napoleon when his nephew died of the condition stimulated many studies of membranous croup in France in the early part of the nineteenth century. Blaud (1823) was possibly the first to mention non-membranous laryngotracheitis, although the Hippocratic writer in the "Coan Prognosis" probably recognized the condition when writing, "Running of the nose and sneezing are bad signs if they precede or supervene upon an infection of the lungs" (Chadwick and Mann, 1950). It was not, however, until the influenza pandemic of 1918, and, following this, the stressing by Thomson (1922) and others of non-diphtheritic infection, that the present interest in and the importance of acute non-diphtheritic laryngotracheobronchitis arose.

The condition was at first the concern of the otolaryngologists in America, and Jackson and Jackson (1936) found a mortality rate of 70% in children under 3 years of age. It would seem that the present mortality of the type of case seen by the surgeon is often still in the region of 50%. Kayser (1941) and Neffson (1944) have well reviewed the progress of the condition as seen in America, and Neffson (1949) refers to over a hundred relevant communications. In this country the condition has received comparatively little comment, and, according to Bonham-Carter (1949), is not generally recognized because of its relative rarity. An epidemic in Dundee was reported by Forfar, Keay, and Thomson (1951), and, apart from this, only small groups have been recorded. Its present clinical state is well summarized by Moncrieff and Weller (1949) when they say, "Laryngotracheobronchitis is one of the most alarming emergencies with which the children's physician has to deal . . . other acute affections of the respiratory tract usually yield to chemotherapy . . . this one . . . is uninfluenced by such treatment."

While the clinical picture of laryngotracheobronchitis is well described and a series of clinical cases is reported by Briggs and Heseltine at page 1064 of this issue, the comparison of mortality rates and results of therapy is almost useless, owing to the different types of cases included in the milder and cured forms. The nomenclature of the condition is confusing, and is studded with dramatic adjectival prefixes such as "obliterating," "suffocating," "obstructive," "stenotic," "fulminating," etc. The pathology of the condition as seen by us does not always coincide with that described by Neffson (1949).

The present communication is an attempt to assess the incidence of mortality of the condition and to discuss the processes which lead to death and against which treatment may be directed.

Material

The material used is from a series of 650 personally conducted necropsies carried out over the last four years in children dying in Sheffield. Most of the cases were from

the Sheffield Children's Hospital, but many of the necropsies were carried out at the request of the coroner, others at the Sheffield City General Hospital, and some at the request of general practitioners.

Definition and Cases.—Under the heading "laryngotracheobronchitis" have been included all the cases of acute affection of the respiratory tract in which death was thought to be due to obstruction to the airway at or below the level of the glottis. Cases with terminal inhalation of regurgitated stomach contents were excluded, as were cases showing bronchopneumonia. A clinical history was available in all cases. In most of these there was a history of up to four days' cold in the head with or without a cough. This was followed by either unexpected death in bed or by a sudden increase in severity of the illness. The interval between the onset of severe symptoms and death varied from a few minutes to three days under treatment. Cases with a similar history but with severe symptoms lasting four or more days all showed bronchopneumonia and were excluded from this group.

Results

Among the 650 necropsies were 119 cases in which bronchopneumonia was found; most of these were terminal and secondary infections. There were 41 cases of chronic lung infection, many of which were associated with inhalation of regurgitated stomach contents. There were 35 cases in which the primary cause of death appeared to be an acute intrinsic affection of the tracheobronchial tract in which the essential feature was obstruction of the air passage. When these latter cases were analysed they fell into five distinct groups (see Table). The case of oedema

Lesions found in 35 Cases of Laryngotracheobronchitis

	No. of Cases	
Oedema of glottis	1	
Upper or laryngeal (Neffson)	2	
Necrotizing:		
Influenzal	1	3
Measles	1	
Virus	1	
Exudative	18	29
Capillary bronchiolitis	11	

of the larynx and glottis was probably of the angioneurotic type. There were two cases of laryngeal infection with subglottic inflammation and ulceration of the mucosa. The lumen of the upper trachea contained a large quantity of mucopurulent material and shed epithelium (Special Plate, Fig. 1).

In three cases there was intense vascular engorgement of the mucosa with extensive necrosis of the epithelium and infiltration of the tissues with lymphocytes. One case occurred during an epidemic of influenza and was associated with intense vascular engorgement of the whole lung. One case occurred in a measles contact, and the appearance of the trachea was highly suggestive of Koplik spots; the subepithelial tissues contained groups of cells with multinucleated cells. The third case showed an appearance very similar to the first. It was associated with an epidemic of influenzal cold at the child's home. It is felt that this group of cases of what may be called "necrotizing" tracheobronchitis was associated with virus infections. Coagulase-positive staphylococci were grown from these three cases at necropsy.

The largest group, comprising 18 cases, showed a feature entirely different from the last group. The epithelium was very rarely shed and the cilia were intact (Fig. 2). The lower trachea and bronchi contained extremely tenacious greyish material which adhered to dissecting instruments. This extended to the smaller bronchi but rarely to the terminal bronchioles, the latter being either distended with gas or collapsed. The exudate in some areas was almost acellular and in others contained sheets of lymphocytes, macrophages, and mononuclear cells (Figs. 3 and 4). Many of the bronchial gland ducts and acini appeared to be dilated with inspissated material. The cases that were clinically of longer standing seemed to have a more cellular exudate, particularly in the smaller bronchi and bronchioles. Owing to the great variability of viscosity and the small quantities of material available it was not possible to measure viscosity by any of the usual methods, but it was found possible to compare secretions, using the torsion balance method for the measurement of the surface tension (Fig. A). It was found that the surface tensions of the material from two cases of exudative tracheobronchitis were much greater than that of water, while those of nine small samples of mucus and purulent fluid obtained from the respiratory tract in other conditions were less than that of water.

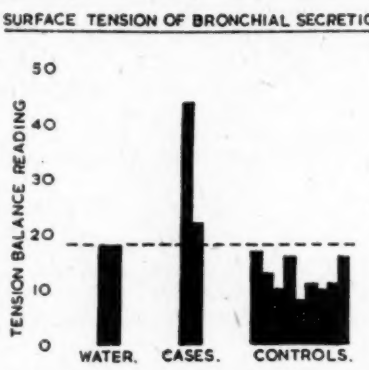

FIG. A.—Chart to show the tackiness of bronchial secretion in two cases of acute laryngotracheobronchitis compared with nine other types of cases and with water.

The final group of cases consisted of 11 children in whom inflammatory changes in the form of purulent fluid in the lumen, cellular infiltration of bronchi and bronchioles, and vascular engorgement were present. In most cases areas were also present where bronchi were filled with mucoid secretion as in the previous group. The term "capillary bronchiolitis" is suitable, as pneumonia in the form of alveolar exudate and infiltration was not obvious. When the clinical histories of the cases in this group and in the exudative group were compared it was found that the preceding histories up to the onset of dyspnoea were similar but that in the group of capillary bronchiolitis there seemed to have been a longer interval between the onset of severe dyspnoea and death.

The ages of the children varied from 6 weeks to 12 years, but if the virus group of necrotizing tracheobronchitis is excluded the ages varied from 6 weeks to 24 months. The age group of the exudative type and the capillary bronchitis appear to be identical. The cases occurred predominantly in the winter months, 33 cases falling between November and April, compared with three cases in the remaining six months.

Cultures were taken from all cases at necropsy, and in some instances also during life. Apart from the three cases of necrotic tracheobronchitis from which pure growths of coagulase-positive staphylococci were isolated, the organisms grown differed in no way from the organisms grown from other routine necropsies.

Discussion

The cases of laryngotracheobronchitis described here were taken from a wide field of material: teaching hospital, municipal hospital, cases reported to the coroner, and others sent in direct from practitioners. Thus they probably give a fair indication of the relative incidence of the affection in an industrial city. The area contains a population of approximately half a million. The number of child deaths in the age group of laryngotracheobronchitis, excluding the influenzal cases—that is, 6 weeks to 24 months—was 167 in 1948; 146 in 1949; and 82 in 1950 (taken from the Annual Reports of the M.O.H.).

The 29 deaths from the exudative affection of the bronchial tree occurred fairly evenly over the four years of study, making approximately seven deaths a year. The total number of reported deaths from pertussis in Sheffield in 1949 and 1950 was 12. The average number of children under the age of 2 years who are reported to have died of pertussis in Sheffield each year during the past few years is approximately 10. The number of deaths from measles is much less. Since the necropsy series studied here comprised

a great deal less than one-third of the children dying in the area, it is probably correct to say that acute laryngotracheobronchitis accounts for more deaths in this age group, 6 weeks to 24 months, than all the generally recognized and notified infectious diseases.

The relatively high incidence of acute laryngotracheobronchitis found in this series is probably due to a deliberate attempt to perform necropsies on "acute deaths" in an endeavour to obtain tissues free from secondary changes. It is probable that, but for necropsy, almost all these cases would have been recorded as "bronchopneumonia."

The single case of oedema of the glottis does not merit discussion. The two cases in which the lesions were chiefly confined to the larynx and trachea, with ulceration, were the only cases in which the findings were similar to those described by Neffson (1949) and Le Jeune and Bayon (1941). These cases had received considerable treatment before death—one several intubations and later aspirations following tracheotomy, and the other several intubations. Thus the ulceration and oedema may well have been related to traumatic procedure, and the primary lesions were probably submerged in secondary changes. This may well also apply to much of the material presented and reviewed by Neffson (1949).

The three cases which showed intense engorgement with necrosis of epithelium, and from which staphylococci were grown, formed a clinical and pathological group in that they were all probably instances of virus infections promoting an influenzal type of reaction. This was the only group containing children over the age of 2 years: one child was aged 3 months, one 5½ years, and the other 12 years. The lesions in these cases seemed entirely different from the exudative affection seen in other groups, and will not be discussed further here.

The two largest groups—that of the exudative type and that with capillary bronchiolitis—are best discussed together, as the capillary bronchitis cases are probably the later stages of milder forms of the exudative type. This view is based on two observations: (1) the length of time between the onset of severe symptoms and death appeared to be much longer in the bronchiolitis group, and (2) examination of the bronchial secretion obtained from cases of the exudative type that survived showed that the early aspiration fluids were chiefly mucus with few cells, and that the later aspirations preceding recovery became more and more cellular, eventually becoming almost purulent and much less viscid.

The clinical condition in these cases seems to be related primarily to the viscous secretion. The sticky glutinous secretion seen in these cases has been well described by Baum (1928) as "drying in a glue-like consistency on the bronchoscope." Our observations on the "surface tension" of the material in a few cases merely gives measurable and recordable confirmation of clinical observations. Knowledge of the normal mechanism of bronchial secretions is remarkably scanty (Cowdry, 1942). It is obvious that extensive fluid exchanges must take place throughout the bronchial mucosa, as the combined circumference of the ciliated epithelium of the bronchioles is several metres and that of the trachea and bronchi a few centimetres (Hilding and Hilding, 1948). The cilia appear to act simultaneously at all areas, particles and fluid being propelled towards the trachea by cilia at a speed of about a centimetre a minute (Hill, 1928).

Florey, Carleton, and Wells (1932) investigated secretion in the trachea and found that vagal stimulation or pilocarpine increased the gland secretion, the action being inhibited by atropine. They found no evidence of nervous control of goblet-cell secretion. Holinger, Basch, and Poncher (1941) showed that whereas carbon dioxide tended to liquefy sputum, oxygen tended to concentrate it and produce mucosal pallor. It would seem that sputum normally undergoes partial liquefaction within the bronchus before expectoration. It is possible that a defect in liquefaction is present in cases of laryngotracheobronchitis. It is likely that bacterial infections play a part in the liquefaction of the mucus in laryngotracheobronchitis, but the relationship of infection to the disorder is not obvious.

Clinically, the acute condition often arises after a running nose or upper respiratory infection—but colds are so common during the winter months in households with children that it would seem that the cold may be incidental or act as a trigger mechanism. A possibly analogous situation is parenteral gastro-enteritis. It has been noted in several cases that the onset of severe symptoms followed the administration of sulphonamides. It seems possible that antibacterial agents may interfere with bacterial growth at a crucial point in an infection and upset the liquefaction of sputum. It must also be pointed out that the condition does not always follow a recognizable upper respiratory tract infection, and that it has followed surgical procedures to the trachea and bronchus such as the removal of an inhaled foreign body (Richards, 1933).

The bacteriology of the condition in our hands has revealed no significant organisms, and the literature on the subject suggests that the affection is unrelated to any particular organism, or is a non-specific reaction to many organisms, or is the result of invasion by an unknown virus. Richards (1933) obtained haemolytic streptococci from his cases; he regarded them as the infective agent, and other organisms as secondary invaders. Connell and Trowbridge (1941) thought similarly. MacCready (1944) thought *Haemophilus influenzae* the likely pathogen, but the high incidence of *H. influenzae* found by Benstead (1950) in bronchial secretion in bronchiectasis is probably relevant here. Arden and Duhig (1944) believed the pathogenic agent to be a virus, but not the influenza virus. They drew attention to the presence of an infective virus tracheitis of chickens (Burnet and Foley, 1941). While an unknown virus may be the causal organism, this cannot be assumed on negative bacteriological findings only—there being no entirely convincing evidence that the disease is primarily an infection.

When infection occurring late in laryngotracheobronchitis is considered two points are prominent. First, the tenacious secretion is replaced by cellular fluid after two to four days; and, secondly, the disorder is almost self-limiting in time. If a child with the disorder lives for more than four days it develops bronchopneumonia, and secondary changes occur within the lung. Chemotherapy is naturally ineffective at the onset of the affection for the obvious reason that the symptoms at this time are largely the results of mechanical obstruction. In a series of cases treated by Briggs and Heseltine (1952) no difference was found between the different antibiotics used, but recovery appeared to occur on or about the fourth day. With their mechanical aspirations the volume of the material they aspirated confirmed the observations of Connell and Trowbridge (1941) that the tenacious secretion continued to be produced for two to three days before becoming liquid. It seems possible that laryngotracheobronchitis is a generalized form of the condition that in other individuals produces lobular collapse. Small areas of bronchi filled with mucous secretion are well known in many long-standing infections of the bronchial tree (Henke and Lubarsch, 1928). The relationship of the lung lesion seen in association with fibrocystic disease of the pancreas is not obvious. None of the cases in the present series showed histological abnormality of the pancreas.

From a functional point of view the pathology of laryngotracheobronchitis may be as follows. In an upper respiratory infection there is catarrhal inflammation which is largely eliminated by coughing and sneezing. If, however, the secretion is excessive or abnormal or the cough mechanism is inadequate a vicious circle seems to develop which, unless relieved, may result in death. Immobility of the lung is known to interfere with the absorption of fluid (Courtice and Phipps, 1946) and anoxia reduces the activity of cilia (Grey, 1928). It is obvious that once this cycle is set up it is unlikely to be influenced by antibacterial drugs unless the secretion is purulent, and such

drugs may in fact, by preventing the growth of secondary bacterial invaders, postpone the bacterial liquefaction of the tenacious secretion. Treatment should be directed primarily to the relief of anoxia, the liquefaction of mucus, and the mechanical removal of tenacious secretion.

Summary

A study was made of 35 children dying of acute laryngotracheobronchitis over a four-year period in Sheffield.

Twenty-nine children died of an exudative affection of the lower respiratory tree.

Laryngotracheobronchitis would appear to be a more common cause of death in children between the ages of 6 weeks and 2 years than the notifiable infectious diseases.

The aetiology of the condition is not known, and the infection is not necessarily specific.

Death seems to be due chiefly to mechanical suffocation by abnormal mucous secretion.

Treatment should be directed to maintaining an airway. Antibacterial drugs are unlikely to be effective in the early stages of the disease and may possibly postpone recovery.

It is a pleasure to acknowledge the interest and advice of Dr. E. H. Harding. The photographs are by A. K. Tunstall.

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The *Hospitals Year Book* for 1952 is a comprehensive guide to regional hospital boards, boards of governors of teaching hospitals, management committees, boards of management, etc. The bed and patient statistics section provides a complete analysis of the allocation of beds in all N.H.S. hospitals. In an introductory article the editor points out that public attention has been so concentrated on financial problems of the national hospital service that its achievements are in danger of being overlooked. In England 40,000 more beds are available than in 1948, and full-time nursing staff have increased by 25,000. Despite such progress the position in mental hospitals and mental-deficiency institutions is acute; 3,000 mental-hospital beds which were diverted to other uses during the war have not yet been brought back into service, and another 2,800 are closed for lack of staff. The *Year Book* is published by the Institute of Hospital Administrators, 75, Portland Place, London, W.1, and costs 45s.

EFFECT OF ANTIBIOTICS ON TISSUE CULTURES OF HUMAN SKIN

BY

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AND

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[WITH SPECIAL PLATE]

As several antibiotics are now available for the treatment of infection by a wide range of organisms, it is useful to consider their relative toxicity to the tissues. This is particularly important when antibiotics are used for local application, as in these circumstances high concentrations may be maintained in contact with the skin. In this unit the practical problem arises which of the antibiotics active against the flora of burns is likely to be least harmful when applied as a local dressing. Clearly the drugs should not inhibit the growth and migration of epithelium in the concentrations used.

A rapid method of assessing the relative toxicity of antibiotics to human skin is provided by the use of cultures of skin *in vitro*. This method does not involve exposing patients to the risk of harmful concentrations of antibiotics, and makes it possible to compare their effects under controlled conditions. In the experiments to be described, explants of human skin cultivated in a fluid medium were used as the test material. These were subjected to various concentrations of aureomycin, terramycin, chloramphenicol, polymyxin B and E, penicillin G, streptomycin, neomycin, and "A18" hydrochloride* in order to determine the highest concentration of each which had no adverse effect upon the growth and migration of epithelium.

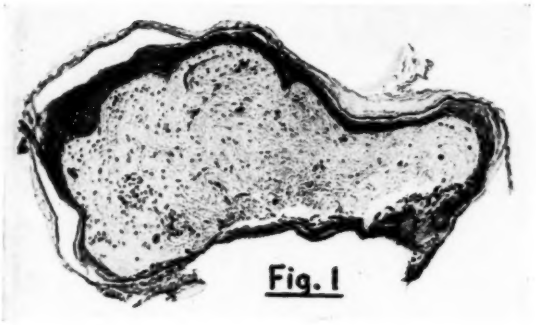
Methods

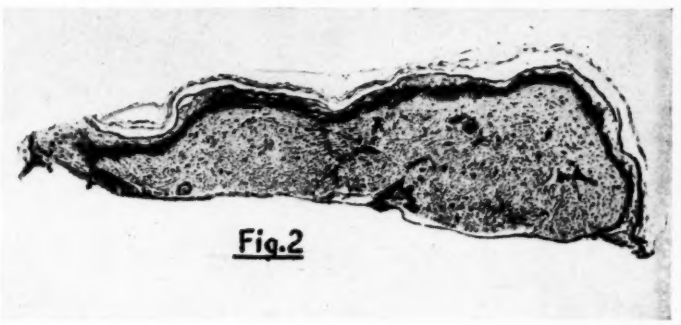
Cultivation of Human Skin in Vitro.—Adult human skin was obtained by using the excess of material which was removed for storage after skin-grafting operations, and was explanted either immediately or within 24 hours of removal. The skin was preferably of medium thickness—that is, containing about the same thickness of dermis and of epidermis. It was cut into small pieces about 1–2 mm.^{2} in size, and cultivated upon the surface of a fluid medium. The method used was a modification of that originally described by Medawar (1948) for the cultivation of adult rabbit skin, which has proved successful for guinea-pig skin (Cruickshank, 1951). Each explant was cultured in 0.5 ml. of medium in a 5-ml. rubber-stoppered bottle, in an atmosphere of 50% oxygen and 50% air at 37° C. The medium consisted of 5 parts fresh homologous serum, 3 parts Krebs–Ringer phosphate, 1 part 5% glucose in distilled water, and 1 part streptomycin (500 units/ml.) in Ringer's solution. Streptomycin in this concentration is free from toxic effects, and is included routinely to prevent infection of the cultures by organisms normally present on the skin surface. During cultivation the explants were rocked through 15 degrees each way from the horizontal about five times a minute on a specially devised platform.

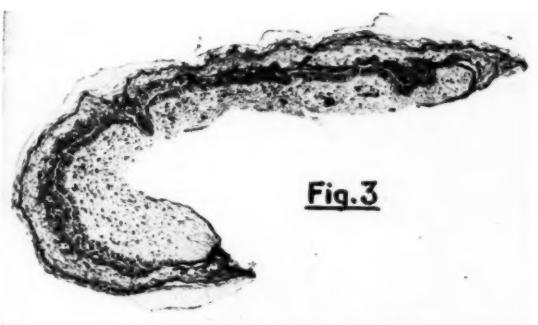
In order to test the effects of the various antibiotics the appropriate solutions of these were substituted for the 1 part

*"A18" is an antibiotic in the process of development by Glaxo Laboratories Ltd.

C. N. D. CRUICKSHANK AND E. J. L. LOWBURY: EFFECT OF ANTIBIOTICS ON TISSUE CULTURES OF HUMAN SKIN







Human skin cultivated for three days. (Haematoxylin and eosin. ×75.) FIG. 1.—Normal control culture. FIG. 2.—Culture showing minor inhibition. FIG. 3.—Culture showing severe inhibition. FIG. 4.—Culture showing destruction of explant.

J. L. EMERY: ACUTE LARYNGOTRACHEOBRONCHITIS IN CHILDREN

FIG. 1.—The lining of the upper part of the trachea, showing destruction of the epithelium and exudation from glands. (Haematoxylin and eosin. ×90.)

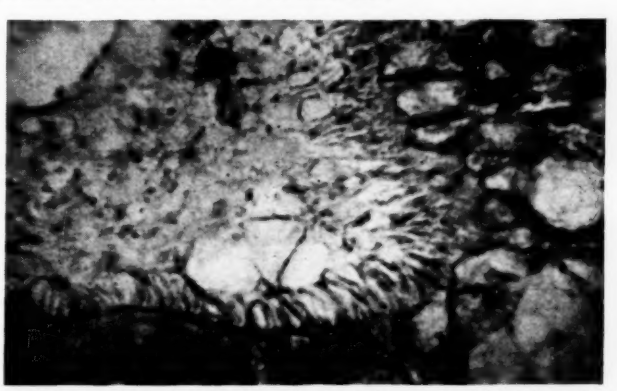


FIG. 2.—Section of the lining of a bronchus of a child dying with the exudative type of acute laryngotracheobronchitis, showing cilia and exudate. (Haematoxylin and eosin. ×700.)

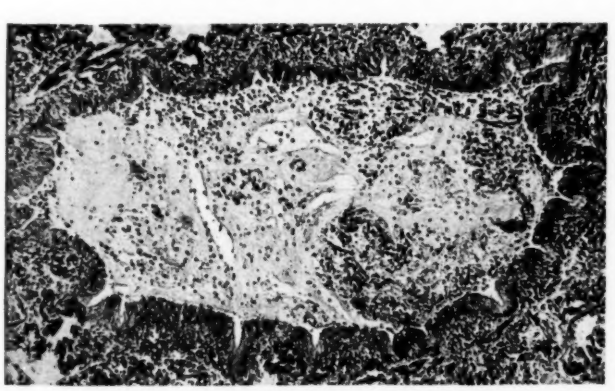


FIG. 3.—Cross-section of small bronchus, showing lumen filled with exudate and small pools of cells. (Haematoxylin and eosin. ×57.)

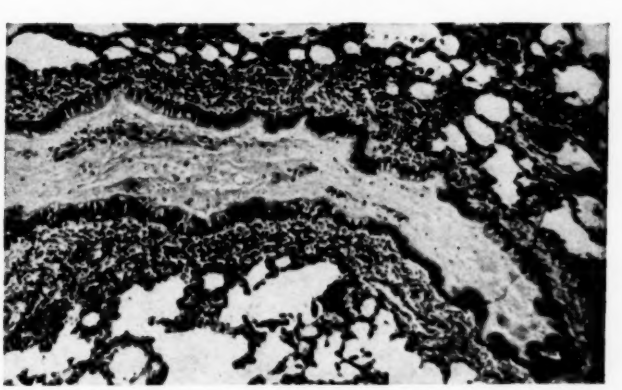


FIG. 4.—A bronchiole cut longitudinally, showing the lumen entirely filled with exudate. (Haematoxylin and eosin. ×60.)

J. G. S. CRABBE: EXFOLIATIVE CYTOLOGICAL CONTROL IN OCCUPATIONAL CANCER OF BLADDER

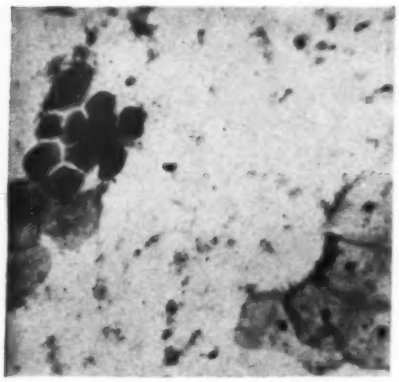


FIG. 1.—Urine deposit smear, showing normal transitional and squamous epithelial cells. (×375.)

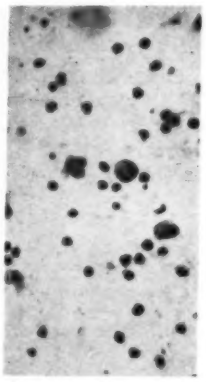


FIG. 2.—Urine deposit smear, showing red and white blood cells, histiocytes. (×375.)

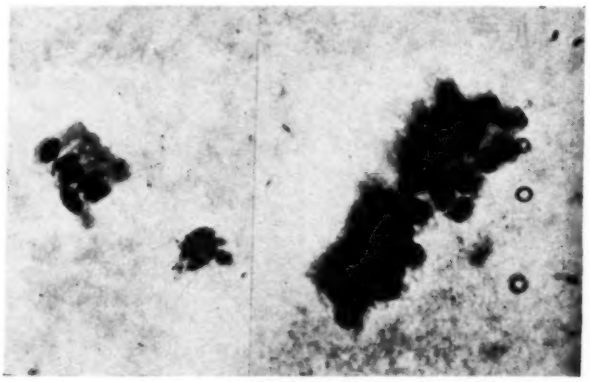


FIG. 3.—Urine deposit smear, showing a group of "benign" papilloma cells with definite palisading. (×775.)

FIG. 4.—Urine deposit smear, showing malignant cells and cell clusters. (×375.)

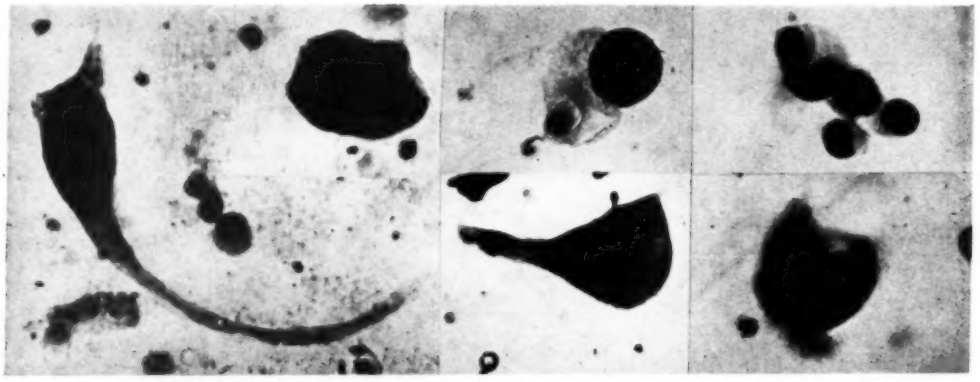


FIG. 5.—Urine deposit smear, showing separate malignant cells in bizarre forms. (×775.)

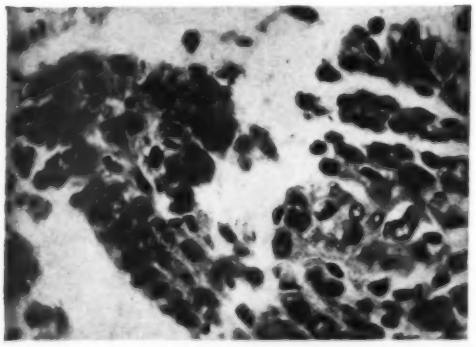


FIG. 6.—Section from the same tumour as Figs. 4 and 5. (×375.)

BETTY WALKER: MILIARY TUBERCULOSIS IN A CASE OF ACUTE DISSEMINATED LUPUS ERYTHEMATOSUS

FIG. 1.—Radiograph of chest before treatment with A.C.T.H.

FIG. 2.—Radiograph of chest in January, 1951: numerous miliary deposits with early confluence of lesions.

FIG. 3.—Radiograph of chest in November, 1951: miliary deposits undergoing calcification.

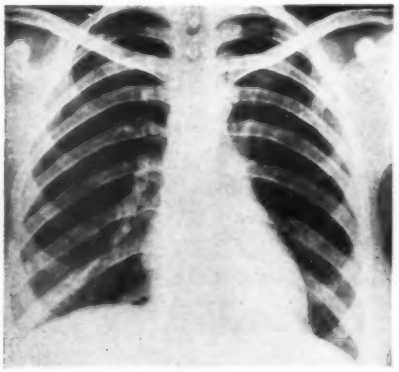


FIG. 1

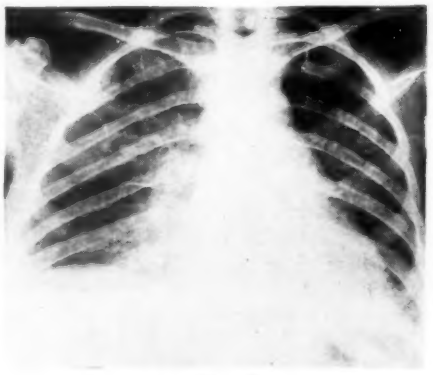


FIG. 2

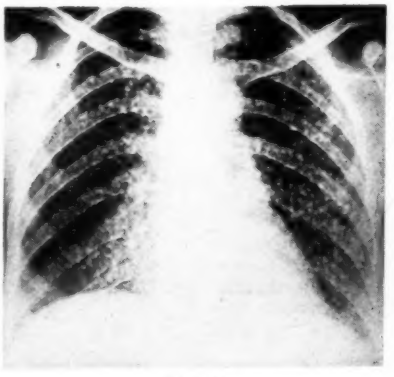


FIG. 3

of streptomycin in the medium. In each experiment the cultures were put up in groups of three—that is, there were three control cultures and three cultures of each of the antibiotics under test.

Standardization of Materials.—Antibiotics were dissolved and appropriately diluted in Ringer's solution, the concentration of the solution added to the medium being 10 times the desired final concentration. The concentrations of the different antibiotics which were tested are shown in the accompanying Table. Aureomycin and terramycin, which were acid in solution, required neutralization by sodium hydroxide. Both of these antibiotics are less soluble at neutrality than in acid solution, and a moderate proportion of aureomycin was undissolved at the two highest concentrations (2 mg. and 1 mg.) in the medium. A small insoluble residue was also present in the highest concentration of terramycin and of chloramphenicol (2 mg./ml.). The solutions of these antibiotics were prepared from the capsules supplied for clinical use.

Effects of Antibiotics upon Cultures of Human Skin

Antibiotic	Concentration (mg./ml.)	No. of Experiments	No. of Explants	Normal	Minor Inhibition	Severe Inhibition	Destruction
Control	—	5	14	14	0	0	0
Aureomycin hydrochloride	2·0	2	6	0	3	3	0
	1·0	1	3	1	2	0	0
	0·2	1	3	3	0	0	0
	0·02	1	3	3	0	0	0
Chloramphenicol ..	2·0	3	10	5	2	2	1
	1·0	2	6	1	3	1	1
	0·2	1	3	1	1	1	0
	0·1	2	5	3	1	1	0
	0·01	2	6	5	1	0	0
Terramycin hydrochloride	2·0	2	6	0	0	0	6
	1·0	1	3	0	0	0	3
	0·2	1	3	0	3	0	0
	0·02	1	3	3	0	0	0
Polymyxin E ..	10·0	1	3	0	0	0	3
	2·0	3	9	9	0	0	0
	1·0	1	3	3	0	0	0
Polymyxin B sulphate	2·0	3	9	0	1	5	3
	1·0	1	3	0	1	0	2
	0·2	2	6	6	0	0	0
Penicillin G ..	6·0*	1	3	0	0	1	2
	0·6	2	6	6	0	0	0
Dihydrostreptomycin sulphate	10·0*	1	3	0	0	0	3
	1·0	1	3	3	0	0	0
Neomycin sulphate	10·0	1	3	0	0	0	3
	1·0	1	3	3	0	0	0
	0·2	1	3	3	0	0	0
"A18" hydrochloride	2·0	1	3	0	0	0	3
	0·2	1	3	0	0	3	0
	0·02	1	3	3	0	0	0

* Equivalent to 10,000 units/ml.

The *p*H of the medium in each culture bottle was roughly checked by B.D.H. indicator papers after three days' incubation and found in every case to be between 7 and 7.6. No bacterial growth was found on blood-agar plates inoculated from tissue-culture media at the same time.

Histological Methods.—After cultivation (usually for three days, but occasionally for shorter periods) the explants were fixed in formol-saline, dehydrated, cleared, and embedded in paraffin. Owing to the small size of the explants the periods required for dehydration and clearing could be considerably shortened. From each explant a median section was cut and stained with haematoxylin and eosin. When the interpretation of any result was doubtful, serial sections through the explant were cut and examined.

Results

Appearance of Normal Cultures.—Under normal conditions of culture, epithelium migrates from the edges of the explant over the cut surface of the dermis, which becomes completely encased in epithelium, so that the explant resembles a cyst. Epithelium migrating from the cut ends of the hair follicles may contribute to this layer, which is at first only one cell thick, but subsequently may increase by cell division until it may be three cells thick after three days. The dermis does not undergo any obvious changes, but appears to survive in a quiescent state (Special Plate, Fig. 1).

Assessment of Inhibition.—By this method of culture inhibition of growth cannot be measured quantitatively, but various degrees are clearly recognizable. For ease of comparison cultures which failed to grow normally have been grouped into three categories:

(*a*) *Minor Inhibition.*—Normal staining properties of epidermis and dermis are retained, but migration of epithelium is less than in the control cultures.

(*b*) *Severe Inhibition.*—The normal staining properties of the epidermis and dermis are retained, but no migration occurs.

(*c*) *Destruction.*—There is no evidence of migratory activity, and the staining properties of the cells of the explant are abnormal.

In some instances the explant becomes completely necrotic. Typical examples of these appearances are shown in Figs. 2, 3, and 4.

Effects of the Antibiotics

These effects are summarized in the Table. Triads of explants exposed to the same material showed close agreement in their appearance after incubation, and replication of results in different experiments was good. The following conclusions can be drawn on the action of the different antibiotics.

Aureomycin.—This did not exercise any harmful effects upon cultures in concentrations of 0.2 mg./ml. or less. Above this level, inhibition of the cultures was usually noticed. In most cases this was not severe—no culture being completely killed. The migration of epithelial cells, however, failed to reach completion. It will be noted that, at concentrations of 1 mg./ml. and above, a saturated solution with some turbidity was obtained.

Terramycin.—This antibiotic was more toxic than either aureomycin or chloramphenicol. At levels of 1 mg./ml. and above, the cultures were consistently killed. At 0.2 mg./ml. the cells survived and some migration took place; at 0.02 mg./ml. normal cultures were obtained.

Chloramphenicol.—The results obtained with this antibiotic were more irregular. Occasionally normal cultures were obtained with concentrations of 2 mg./ml., but again at 0.1 mg./ml. abnormal cultures were sometimes present. Variation in the source of the test material may partly account for the irregularity, but even within single experiments inconsistencies were noted. These inconsistencies make it difficult to assess the toxic level of this drug, but it can be concluded that concentrations higher than 0.01 mg./ml. are apt to prove toxic.

Polymyxins E and B.—Polymyxin E appeared to be slightly less toxic than polymyxin B. The former killed cultures at 10 mg./ml., but normal cultures were obtained at 2 mg./ml. and below. On the other hand, polymyxin B caused either death or severe inhibition at 1 mg./ml., but consistently normal cultures were obtained at 0.2 mg./ml. and below. Some of the cultures containing non-toxic amounts of the polymyxins showed forms of growth which differed from those of the normal culture. There seemed to be a stimulating effect on the epithelium, which grew out into a thick layer. Further investigations are being carried out upon this phenomenon.

Penicillin G.—6 mg./ml. (10,000 units/ml.) was toxic to skin in culture, but normal cultures were obtained at 0.6 mg./ml. (1,000 units/ml.).

Streptomycin.—10 mg./ml. proved toxic, but normal cultures were obtained at 1 mg./ml.

Neomycin.—10 mg./ml. caused either death or severe inhibition of the cultures; 1 mg./ml. allowed skin to grow normally.

"A18" Hydrochloride.—No normal cultures were obtained at 0.2 mg./ml. and above, but normal growth proceeded at 0.02 mg./ml.

Discussion

Caution is necessary in interpreting these results for clinical purposes. Although the proliferation of skin in the cultures described may be compared to that of skin over burns involving epidermis only, the effect of substances on tissue culture probably gives an overestimate of their toxicity *in vivo*. Any antibiotic applied to the surface of a wound is continuously diluted by the tissue fluids which are exuded, and is also removed from the site of application into the blood stream. Nevertheless, the relative toxicity of different antibiotics to the skin can probably be assessed by the method described. It is possible, however, that the toxic effects of aureomycin are somewhat underestimated in comparison with those of other agents, because of its instability at the *p*H and temperature of incubation used in the tests.

As penicillin has been used in this unit for several years as a routine for local application to burns, it is interesting to consider its toxicity to skin as shown by tissue culture. *In vitro*, 1,000 units (0.6 mg.)/ml. did not harm skin, while 10,000 units (6 mg.)/ml. caused severe inhibition or death of cells. When applied to burns, 1,000 units of penicillin per ml. has been found to have no harmful effects. For a short period a cream containing 10,000 units of penicillin per g. was applied to burns colonized by *Str. pyogenes* (Jackson *et al.*, 1951) and no ill effects were observed in individual cases. The tissue-culture tests would appear, in this instance, to overestimate the toxicity of penicillin G to epithelium. It is possible, however, that the higher concentration of penicillin might cause a minor degree of interference with healing, which could be detected only by comparing the healing times of a large number of treated cases with those of a comparable control series.

Another factor which must be considered in interpreting the results of these experiments for clinical purposes is the solubility of the antibiotic in tissue fluids. There is greater risk in using a high concentration of an antibiotic when it is very soluble than when it is relatively insoluble. For example, a saturated solution of aureomycin at an approximately neutral reaction does not cause any severe inhibition as judged by the present tests. On the other hand, polymyxin will easily dissolve in a concentration of 10 mg./ml., and at this level it is decidedly toxic to skin *in vitro*. Similarly, penicillin G will form solutions considerably stronger than that which will prevent the growth of epithelium in culture.

Lépine *et al.* (1950) tested the effect of aureomycin and of chloramphenicol on explants of chick embryo lung, and found that proliferating epithelial cells and fibroblasts were retarded in growth by 0.01 mg./ml. and completely inhibited by 1 mg./ml. of these substances. It is probable that the difference between these findings and those reported above can be attributed to the nature of the test materials. Adult human tissue which was used in the present experiment might reasonably be expected to show effects more comparable to those which occur in healing human burns.

Reports are available concerning the effects of penicillin and streptomycin on cells in culture. Both of these antibiotics are regarded for tissue-culture purposes as being non-toxic to normal cells at concentrations of 100 units/ml. (Cameron, 1950). It will be noted that in the present experiments the maximum non-toxic level is set higher at 1,000 units/ml. It must be understood, however, that the object of these experiments is to determine the maximum non-toxic level, with particular relation to clinical treatment, and that where there is a safe margin between toxicity and bactericidal properties it is clearly desirable for tissue-culture purposes not to exceed the bactericidal concentration more than is absolutely necessary.

Summary

The effects of varying concentrations of a range of antibiotics upon human skin cultivated *in vitro* are described.

By this method the highest concentrations of these substances free from toxic effects are assessed as follows: aureomycin hydrochloride, 0.2 mg./ml.; terramycin hydrochloride, 0.02 mg./ml.; chloramphenicol, 0.01 mg./ml.; polymyxin E, 2 mg./ml.; polymyxin B sulphate, 0.2 mg./ml.; penicillin G, 0.6 mg./ml. (1,000 units/ml.); dihydrostreptomycin sulphate, 1 mg./ml. (1,000 units/ml.); neomycin sulphate, 1 mg./ml.; "A18" hydrochloride, 0.02 mg./ml.

The relationship of these results to the clinical effects of local applications of antibiotics is discussed.

We wish to acknowledge the technical assistance of Mr. J. R. Cooper and Miss M. Hulse, and to thank Glaxo Laboratories Ltd., Burroughs Wellcome and Co., and the M.R.C. Antibiotics Clinical Trials (Non-Tuberculous Conditions) Committee for providing antibiotics.

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EXFOLIATIVE CYTOLOGICAL CONTROL IN OCCUPATIONAL CANCER OF THE BLADDER

BY

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[WITH SPECIAL PLATE]

The relative ease with which exfoliation of cells occurs from bladder tumours into the urine has been noted by Papanicolaou (1947, 1948) in the day-to-day cases of unknown aetiology, and by Goldblatt (1947) in cases of known aetiology in the dyestuffs industry. The utilization of this fact in the early diagnosis of bladder tumours in workers is the subject of this paper.

Whereas American authors have repeatedly emphasized (Papanicolaou, 1947; Fremont-Smith *et al.*, 1948) that exfoliative cytological diagnosis must be regarded as an adjunct to the more usual procedures (cystoscopy, biopsy, *x*-ray examination), the situation is somewhat different in the consideration of occupational bladder tumours in this country. Routine cystoscopy is stated to be practised in America, Switzerland, and Italy (Müller, 1951; di Maio, 1937, 1949; Barsotti and Vigliani, 1949) in factories where occupational bladder tumours have arisen among workers in certain departments that manufacture or use dyestuffs intermediates. Such a routine, at intervals of say six or twelve months, is the best if not an infallible way to detect tumours at a stage early enough to ensure hopeful or successful treatment.

In Britain, routine cystoscopy has never commended itself (Goldblatt, 1947) to workers. Only when, by the repeated and increasing appearance of red blood corpuscles in the urine, the presence of a tumour is rendered probable are workers amenable to persuasion and agree to undergo cystoscopy before and periodically after appropriate operation or treatment. This is quite understandable, inasmuch as the workman experiences

no symptoms in the early stages, and may, in spite of previous instruction in the nature of the occupational hazard, be unable to visualize a process which is asymptomatic. The term "tumeurs silencieuses" (Billiard-Duchesne, 1947) graphically evokes this fact. Such persuasion is often necessary even before the occurrence of visible haematuria, when repeated detection of even a few red blood cells miscroscopically in the urine lends probability to the presence of a tumour.

The disadvantage of reliance on the detection of haematuria as a criterion of tumour of the bladder is that it is often too late a sign to render surgical measures hopeful. In some cases of occupational bladder tumour even microscopy fails to reveal haematuria before infiltration of a malignant process into the vesical muscle has occurred.

The inverse situation of microscopic or even visible haematuria without an attendant tumour is not uncommon among workers who have accidentally absorbed (through the skin or by inhalation) certain aromatic amines and derivatives of them (Goldblatt, 1947, 1949b). In such cases of haemorrhagic cystitis exfoliated and apparently normal bladder cells are detected in the urine.

It will be apparent that the need is for some examination which permits recognition of a tumour at the earliest possible stage in the medical supervision of workers who, as a result of repeated exposure to certain aromatic amines years ago, when working conditions were bad, may at any time manifest a neoplastic process in the bladder, or who may develop a recurrent tumour process after previous treatment.

In day-to-day hospital practice it is inevitable that the cases should come to the notice of the urologist only when the neoplastic process (innocent or malignant) has obtruded itself upon the patient or on the attention of his medical attendant. By this time the tumour is established and may already be at an advanced stage of development.

To make detection possible at an early stage it would be necessary to examine all urine samples taken in hospital by a cytological technique of a kind similar to that so successfully applied by Papanicolaou and Traut (1943) in the field of cervical and other tumours. The application of these ideas to factory workers, among whom it is certain that some bladder tumours will be found and from whom routine urine samples can be obtained regularly, commends itself at once, especially if, as is the case in this country at least, routine cystoscopy of workers is not feasible. The detection of exfoliated cells indicative of or raising the suspicion of neoplastic or pre-neoplastic origin even in the absence of all other signs or symptoms would logically lead to cystoscopic investigation.

Whereas, as pointed out by Schmidlapp and Marshall (1948), "false positive reports are especially undesirable," such results among dyestuffs workers are much less undesirable than false negatives. False positives arise from the misinterpretation of appearances. But, as will be seen, "false" positives can sometimes be more reliable than the cystoscopist, and may, after repeated efforts, be vindicated by the discovery of a small and secluded tumour.

If a neoplasm is present it is very probable that cytological examination of a number of specimens of urine over a relatively short period will yield positive results. The difficulties encountered are considered below. It is thus apparent that the number of initial cystoscopic examinations will be diminished, since they will, in general, follow only when the cytological report indicates their necessity. Experience has already shown that the number of such examinations has been diminished by half, and that positive cases have been detected in the absence of microscopic haematuria.

Material

The factories in which these studies of urine sediment cytology were carried out were for the most part those from which the cases collected and analysed by Goldblatt (1949a) were obtained. The description of the operations performed in these factories by him applies, except that the amelioration of working conditions and improvement of chemical processes have advanced even further.

The material was placed at my disposal by Dr. Michael H. C. Williams, his colleague, Dr. Charles Cresdee, and Dr. T. S. Scott, and they, as well as workers and plant managers, helped to establish the complicated arrangements necessary to obtain specimens of urine from the workers and to be certain of their identification. During the past year the urines from about 1,000 dyestuffs workers have been examined by the Papanicolaou technique (1942). The co-operation of Mr. Poole Wilson and his staff at the Urological Department of the Salford Royal Hospital was essential to the progress of the work and was freely given.

Technique

Urine is collected in a numbered vessel and an equal volume of 95% ethanol or industrial alcohol is added. About 40 ml. of this mixture is centrifuged for 15 minutes at 2,000 r.p.m. After the supernatant liquid has been poured off, smears are either made at once or the deposit can be kept for some days in a refrigerator, a little absolute ethanol having been first added. Smears are made by spreading a small amount of the urine deposit with another cleansed slide on numbered slides which have been washed in ethanol, polished, and smeared with albumin in glycerol. When the smear begins to cloud slightly round the edges or in its thinner parts the slide is placed in fixative (95% alcohol and ether, equal volumes). The smear must not be allowed to dry at any time.

The Staining Process.—Fixative→80% (15–30 seconds)→70%→50% EtOH→distilled water→haematoxylin 2 minutes→distilled water→distilled water→50% EtOH→3% NH_4OH in 70% EtOH→70%→80%→95% EtOH→orange G 1½ minutes→95%→95% EtOH→Papanicolaou EA 65 polychrome stain, 1½ minutes→95%→95%→100% EtOH→equal parts EtOH + xylol→xylol (three changes)→mount in Canada balsam→apply cover slips and allow to dry for at least one hour.

Using a binocular microscope with a mechanical stage, objectives ×10, 16 mm., ×40, 4 mm., and wide-field eyepieces ×10 and ×15, the smear is examined under the low power by starting from a marked end of the slide and moving on from each transverse sweep until the whole slide has been traversed. Any doubtful or unusual cells are scrutinized under high power. Areas containing suspicious cells or clusters of cells are located by an appropriate marking for detailed study.

The recognition of significant cells in the smear requires a thorough familiarity with the variability of normal cells and of all non-tumour cells that may be present. This must be combined with an experienced eye for the criteria of malignancy laid down by Papanicolaou (Papanicolaou and Traut, 1943), which may be summarized as follows.

The Criteria of Malignancy

There is no one single criterion of malignancy. These criteria must be used in combination, a sufficient number of them being accepted by the experienced eye as indicative

of neoplastic change. A diagnosis of malignancy is never made on the presence of one cell or cluster of cells only.

In the words of Papanicolaou (1947): "A conclusive positive diagnosis should be based as much as possible on clusters of malignant cells or small fragments of cancerous tissue and not on single exfoliated cells. The criteria are not exclusively cytologic (structural abnormalities of the nucleus and of the cytoplasm), but also histologic (anisocytosis, and anisonucleosis, crowding of cells, irregular pattern, etc.)." This dictum of Papanicolaou's is reminiscent of that of Dudgeon and Wrigley (1935) in reference to their diagnosis of pulmonary tumours by the application of the wet-film method to particles of tissue in the sputum. They stated that "we never made a diagnosis of new growth unless plaques or clusters of malignant cells were seen."

In spite of these dicta, however, it is possible to make a positive diagnosis of a smear which shows only individual cells, each of which possesses a sufficient number of the criteria given below. This has certainly been the case in our experience of smears from urine. In the present series of cases most of the confirmed smear diagnoses showed only individual malignant cells, and in one or two cases only about 10 malignant cells were visible in each smear.

Papanicolaou's criteria are: (1) Enlargement and prominence of the nucleus. Alteration of the nuclear-cytoplasm ratio. (2) Alteration of the chromatin pattern. (3) Increase in the chromatin and hyperchromasia. (4) Abnormal shape of the nucleus. (5) Anisonucleosis (variation in nuclear size in a group of cells). (6) Enlargement and increase in the number of nucleoli and karyosomes. (7) Increase in size of cells. (8) Bizarre cell shapes. (9) Mitotic figures are very rarely seen in exfoliated cells, but are significant when seen.

Classification of Cells Seen in the Smear

Since cells at all stages of development from normality to malignancy may be seen in a smear, Papanicolaou introduced a system of grading which permits both a finer classification of cells and a safety margin where doubt is experienced (Table I).

TABLE I.—*Papanicolaou's Grading*

Class	Diagnosis	Characters of Cells in Smear	Tumour Possibly Present in Bladder
I	Negative	Normal cells only	None
II	,,	Atypical but not malignant	Papilloma (?)
III	Suspicious	Abnormal but not conclusively malignant	Papilloma, papillary carcinoma?
IV	Positive	Cells and clusters highly suggestive of malignancy	Carcinoma
V	,,	Cells and clusters without doubt malignant	,,

The discovery of the presence of Class IV and V cells must be followed by cytoscopy. The presence of Class III cells calls for repeated re-examination at short intervals. The presence of Class II calls for re-examination at more frequent intervals than heretofore.

Since Dean (1948) has stated that "the detection of benign papillomata by the method as at present applied therefore is of little value," it is important to note that Schmidlapp and Marshall (1950) emphasize that "by far the greater number of papillomata are reported in Class II." Dean's figures seem discouraging for benign papillomata. He found that in a group of 36 patients with histologically proved benign bladder tumours the smear reports were:

Classes I and II	27; no malignant cells
Class III	8; suspicious cells
Classes IV and V	1; malignant cells

It is not clear whether the urines (male and female) were repeatedly examined. Probably they were not. If, as would be the case were all these patients under factory control, urine samples were repeatedly obtained, it is highly probable that the number of false negatives would become negligible in a short time, or, put otherwise, that the number of tumours which would escape cytoscopy would be practically zero.

Cells Seen in Smears from Normal Urine

In smears from normal men's urine it is unusual to find more than three or four transitional cells, but occasionally a large number of *normal cells* of all types are seen.

1. *Squamous Epithelial Cells (in Voided Urine)* (Special Plate, Fig. 1).—These may derive from the fossa navicularis, and are present in large numbers if the prepuce is long. They are also numerous if the patient is having oestrogen therapy for carcinoma of the prostate. In female urine they are, of course, very numerous.

2. *Transitional Epithelial Cells* (Fig. 1).—These show a great variation in size, in shape, and in many other ways, which may be due to the fact that in section the normal transitional epithelium shows cells having a variety of shapes and sizes, some of which are multinucleated. Also the cells are soaking in urine before, during, and after exfoliation, which may cause them to swell and become vacuolated. These cells form the lining of very muscular organs and are being continually distorted and stretched. The normal cellular variations seen are: variation in size of the cells; vacuolation of cytoplasm; bi- and multi-nucleation; variation in size of the nucleus; and clusters of vacuolated cells. In these cells, however, the nucleus shows no hyperchromasia and has a fine, evenly distributed chromatin network, often palely staining, and the nuclear cytoplasmic ratio is always within normal limits. The cytoplasm often shows a well-defined ectoplasm and endoplasm, and sometimes there may be 20 nuclei or more in a single cell.

3. *Renal Cells from the Collecting Tubules.*—These are small round cells, about twice the size of a polymorph, with deeply staining cytoplasm and a small round dark nucleus; they are sometimes seen in clusters of a cast-like formation.

4. *Leucocytes* (Fig. 2).—Polymorphs and lymphocytes. Histiocytes:—These are usually smallish cells, though they can vary considerably in size. They have a deeply staining frothy cytoplasm and often contain ingested particles, among which can sometimes be seen one or two phagocytosed red blood cells. The nucleus is usually small, dark, spherical or oval in shape, and eccentrically placed, and may be multiple.

5. *Red Blood Cells* (Fig. 2).—These are seen occasionally.

Atypical but Non-malignant Cells in Smears

A number of conditions such as infection and renal or vesical calculi can give rise to metaplasia and produce atypical cells which can easily be confused with malignant cells by the inexperienced technician. Erythrocytes, leucocytes, mucus, and crystals, if present in quantity, can all interfere with the staining reaction and confuse the cytological picture.

Cellular Picture in Cases of Neoplasm

"Benign" Papillomata.—The cells from these tumours are columnar, and appear singly or in clusters which show palisading. They are fairly small, with round or oval palely staining nuclei situated at one pole of the cell, and show none of the criteria of malignancy (Fig. 3).

Carcinomata.—The cells from these tumours show the criteria of malignancy given above (Figs. 4 and 5).

Advantages of the Smear Method of Detection

1. It often permits recognition of the presence of a tumour in the very early stages. Growths, when extensive and relatively far advanced, often do not give such good results with the smear technique because they are likely to have undergone degeneration, ulceration, and sloughing.

2. Positive results may be found in the absence of all other signs—for example, haematuria.

3. When applied to urine it offers no physical disturbance to the workers, and can be repeated as often as may be necessary.

4. Stained and mounted smears can be kept indefinitely for future comparison, and, further, these can be compared and correlated with any pathological sections of biopsy material obtained at operation, as illustrated in Fig. 6.

Disadvantages of the Smear Method

1. Since for the satisfactory screening of large numbers of dyestuffs workers, three or four times a year at least, many hundreds of slides must be very carefully scrutinized, it is apparent that several technicians must be methodically trained, relatively expensively equipped, and given suitable laboratory space.

2. The alternative methods of collecting and fixing specimens in the factory and sending them to a competent cytologist in hospital or sending the worker to the hospital periodically will be found, in general, unsatisfactory. Inconvenient as it may be, it is essential that the work should be done in the factory. Urine examinations are properly a part of the life of a dyestuffs factory. Only those who are in daily contact with the workers can develop the required personal interest in the vital business of screening the urines.

3. Negative findings on a single occasion do not exclude a tumour. It may be necessary to examine many urine smears at different times before the presence of a tumour, especially a "benign" tumour, is reported.

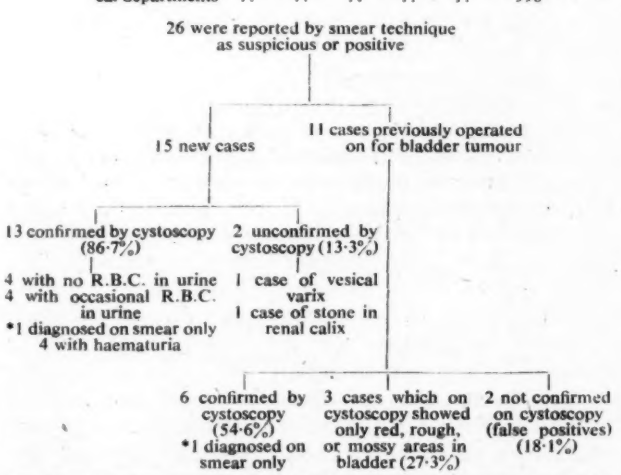
4. If the method in its application to workers is time-consuming, this is not incommensurate with the very important results that are attainable.

Results

In Table II an analysis is given of the results of the examination of the urines of 1,000 men. Table III presents the results of various diagnostic procedures on cases of vesical tumour.

TABLE II

No. of men whose urines were studied	1,000
No. of these men whose urines were examined for red blood cells as a routine at the factory medical departments	998


26 were reported by smear technique as suspicious or positive
15 new cases
11 cases previously operated on for bladder tumour
13 confirmed by cystoscopy (86·7%)
2 unconfirmed by cystoscopy (13·3%)
4 with no R.B.C. in urine
4 with occasional R.B.C. in urine
*1 diagnosed on smear only
4 with haematuria
1 case of vesical varix
1 case of stone in renal calix
6 confirmed by cystoscopy (54·6%)
*1 diagnosed on smear only
3 cases which on cystoscopy showed only red, rough, or mossy areas in bladder (27·3%)
2 not confirmed on cystoscopy (false positives) (18·1%)

* These two cases had never been included in the routine urine examinations for red cells which had been established years before.

It will be seen in Table II that 5 out of the 13 cases confirmed by cystoscopy and 1 out of the 6 "recurrence" cases confirmed by cystoscopy were diagnosed on the smear technique alone. It is on these six cases that we wish to place great stress, for it is on the discovery of such cases that the recommended use of the smear technique rests. The reference numbers of these cases as seen in Table III are H5, H8, H6, C28, A2, and BRes. There is no doubt that but for the cytological diagnosis these cases would not have come to operation until a much later date. The exact amount of time gained is at the moment unpredictable.

TABLE III

No.	Red-cell Test	Smear Test and Class	Cystoscopy Report	Histological Report on Section of Tumour
		New Cases		
B33	None	Malignant IV	Early carcinoma	Papilloma and anaplastic carcinoma
B25	,,	,, V	Multiple papillomata	—
B91	,,	,, V	Small papilloma	Malignant papilloma
C29	,,	,, IV	Carcinoma	Squamous-cell carcinoma
H5	Occasional	,, IV	Carcinoma of apex	Transitional cell carcinoma
H8	,,	,, V	Small papilloma	—
H6	,,	,, V	Carcinoma	—
C28	,,	,, V	Multiple papilloma	Malignant papilloma
H19	,,	,, V	Small varicosity	—
C38	Present	Suspicious III–IV	N.A.D. Stone in ureter	—
H9	Increasing	Malignant IV	Malignant papilloma	Malignant papilloma
H1	,,	,, V	Papilloma	—
A1	Haematuria	Papilloma IV	,,	—
C48	,,	,, IV	,,	Transitional papilloma
A2	Not done	Malignant V	Malignant papilloma	,, ,,
		Men who have had Tumours in the Past		
BRes	Not done	Malignant IV	Papilloma	Pyuria
BEng	Haematuria	Papilloma IV	,,	
B37	Present	Malignant V	Rough red area	
H92	,,	,, V	Inoperable carcinoma	
H4	,,	,, V	Mossy-looking area	
C19	,,	Malignant papilloma V	Papilloma	
H28	,,	Malignant IV	Mossy area	
H7	,,	,, V	Carcinoma	
H89	,,	,, V	N.A.D. (?diverticulum)	
H2	,,	,, IV	Carcinoma	
H3	,,	,, V	N.A.D.	

It will be noted in Table III that in seven cases the cystoscopic diagnosis was papilloma or multiple papilloma, whereas the smear report was malignant, and that in two cases (B91 and C28) the histological report on the tumours was malignant papilloma.

Difficulty arises quite frequently in obtaining the full histological report on the tumour tissue because the urologist may, having seen a papilloma, often proceed to fulgurate it at once rather than try to get a biopsy specimen. The presence of cryptic malignancy may thus be missed.

It is of interest to note that in case H19 the smear report was "malignant," whereas the cystoscope showed only a small varicosity. In spite of this negative cystoscopic result, repeated examinations of urine smears have shown the persistent presence of malignant cells. Only the future can show what the final judgment may be.

Attention must also be drawn to cases B37, H4, and H28, in all the urines of which malignant cells were seen and the cystoscopic reports of which were "rough red area," "mossy-looking area," and "mossy area." These three cases, all having had bladder tumours at some time, were found in the factory routine examination *to have persistent microscopic haematuria.* The finding of malignant cells on the smears on three consecutive occasions seemed to clinch the diagnosis, but, as stated, cystoscopy *did not* show tumours but merely somewhat abnormal areas. Time alone can decide whether on these dubious areas tumours will later be manifest.

In respect of the two "false" positives (H89 and H3), similar remarks apply, cystoscopy up to date being negative in spite of positive reports on smears obtained on three consecutive occasions and repeated microscopic haematuria. The false positive case C38 arose through a manifest misinterpretation of appearances. So far one false negative result has been recorded. This occurred in a man who had previously had a tumour. Two smears of his urine

were examined over a period of three months. They contained no atypical or abnormal cells, but on review cystoscopy a small papilloma was discovered in his bladder.

Ideally, in order to reduce the risk of false negatives to a minimum, the urine should be collected on rising, should be fresh when examined, and at least four smears should be studied from each deposit.

Since the Papanicolaou staining method does not always show red blood cells clearly even when these are present in considerable numbers, it is desirable to devise new fixing and staining methods whereby both *tumour cells* and *blood cells* can be well seen in the same preparation.

Summary and Conclusions

The Papanicolaou smear technique for the detection of tumour cells has been applied to the urines of 1,000 workers in three dyestuffs factories where there was a hazard due to carcinogens.

Twenty-six cases were reported as suspicious or positive. Of these, 19 (73.1%) were confirmed by cystoscopy, 3 (11.5%) were suspicious on cystoscopy, and 4 (15.4%) were false positives. There has up to date been one false negative result.

Six of these cases were diagnosed and confirmed by cystoscopy in the absence of haematuria or other signs of bladder disease. These cases lend great weight to the method.

Experience has shown that the presence of a tumour can be diagnosed on the appearance in a smear of a number of single cells, not necessarily arranged in clusters.

The diagnosis of a tumour cell rests upon a combination of cytological criteria and requires much training and experience.

It is thought that the smear method should be applied extensively in factories where there is reason to believe that the workers have been exposed to bladder carcinogens.

It is not recommended that the search for microscopical haematuria should be abandoned. The two tests should run in parallel.

By applying the smear technique to cases in which possible recurrence must be sought for years, it may be possible to reduce the number of periodic review cystoscopies. It has already been possible to reduce the number of first cystoscopies by about half in the factories referred to.

It is a pleasure to express my thanks to Mrs. Dorothy Moran and to Miss Lucy North for their help in many of the technical operations, to Mr. K. D. Cooper for taking the photomicrographs for me, and to Dr. Alexander Munn for helpful co-operation. I wish to thank Dr. M. W. Goldblatt, head of the Industrial Hygiene Research Laboratories, at whose instance this work was carried out, and who has assisted in the preparation of this paper.

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MILIARY TUBERCULOSIS IN A CASE OF ACUTE DISSEMINATED LUPUS ERYTHEMATOSUS TREATED WITH A.C.T.H.

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[WITH SPECIAL PLATE]

Knowledge of the therapeutic response to A.C.T.H. and cortisone has outstripped understanding of those diseases benefited by their action. It is significant that the introduction of these steroids comes at a time when a new concept of medicine—namely, the body's reaction to disease rather than to individual diseases—is taking the place of the older aetiological notions. Klemperer, Pollack, and Baehr (1941), in making a pathological analysis of 20 consecutive cases of acute lupus erythematosus, showed that the common denominator of the multiform lesions was degeneration of the collagen connective tissue. They pointed out that the same common denominator was present in lesions of rheumatic fever, scleroderma, and periarteritis nodosa. The establishment of a group of diseases on the grounds of a common morphology prepared the way for a mode of treatment unhampered by aetiological considerations. The reports of the physiological effects of A.C.T.H. and cortisone on tissue and tissue changes, and the subsequent release of these steroids for clinical trial, provided the means and opportunity.

It was not surprising that some of the first patients to whom these steroids were administered were sufferers from acute lupus erythematosus. In the beginning it seemed as if the treatment of this hitherto fatal condition would be revolutionized. But in the past two years reports in this country and from America suggested that, despite the prompt and striking remissions in clinical manifestations, the disease process continued. Soffer, Levitt, and Baehr (1950), in a series of 14 patients with three deaths, reported that renal abnormalities and anaemia persisted in all cases, leucopenia in 10, and the "lupus erythematosus cell" in 13. Similar conclusions were reached by Brunsting, Slocumb, and Didcot (1950), in a series of seven patients with three deaths. The initial fall in the E.S.R. was not sustained. The low serum proteins in some cases after clinical remission returned to normal, but the raised alpha$_2$-globulin remained unchanged (Reiner, 1950).

Short remissions of three to four months were reported, but it was agreed generally that most patients required a maintenance dose. Attempts to discontinue treatment in the hope of a natural remission induced a severe exacerbation of the disease.

Shortly after the first enthusiastic accounts of the therapeutic trials with A.C.T.H. and cortisone came reports from Hart and Rees (1950) and Michael *et al.* (1950) that cortisone enhanced the evolution of tuberculosis even in those animals who possessed a high natural resistance to the disease. McNee (1950), commenting on the physiological responses to these steroids, stated that wounds showed no signs of healing and abscesses no signs of granulation-tissue formation in animals or patients to whom they were being adminis-

tered, and warned that their effect on the granulation-tissue barrier around an active tuberculous lesion might be disastrous.

On the other hand, Lurie *et al.* (1951) demonstrated that rabbits of high genetic susceptibility to tuberculosis reacted with certain of the pathological responses characteristic of naturally resistant rabbits when treated with cortisone.

Le Maistre and Tompsett (1950) failed to obtain evidence of enhancement of an experimental tuberculous process in guinea-pigs over a fourteen-day period, using very large amounts of A.C.T.H. and cortisone. They subsequently (Le Maistre, Tompsett, *et al.*, 1951) noted striking benefits from administration of A.C.T.H. to four patients suffering from advanced laryngeal tuberculosis, with improvement in phonation, disappearance of dysphagia, and recession at the site of the lesion.

Thorn *et al.* (1950), in a review on the clinical usefulness of A.C.T.H., mentioned three patients with tuberculosis who showed symptomatic improvement. Freeman *et al.* (1950) reported two similar cases; in one, however, there was a definite spread of the disease during the period of administration.

The reports of activation or spread of tuberculous infection in patients receiving A.C.T.H. or cortisone for other diseases have been surprisingly few, taking into account the large numbers who have been treated with these steroids, both in this country and in America. Three cases of miliary spread demonstrated *post mortem* have been described (Ferriman and Wilsdon, 1950, and Ferriman, 1951; Kleinschmidt and Johnston, 1951; Doerner *et al.*, 1951). Prunty (1952) has reported fatal recrudescence of an apparently quiescent apical lesion in a case receiving both A.C.T.H. and cortisone. It is interesting that two of these four cases were suffering from acute disseminated lupus erythematosus. A third instance is the subject of the following case report.

Case Report

The patient, a housewife aged 35 with two children, was in satisfactory domestic and financial circumstances.

Past History.—Measles, mumps, whooping-cough in childhood. Convulsions on two occasions, at age of 18 months and 9 years. Scarlet fever at 21. Normal pregnancies and confinements. Attended London Chest Hospital for three months in 1947 for recurrent bronchitis; three chest films taken at that time were found to be normal. During the eighteen months before the onset of her acute illness she had suffered from a series of recurrent boils. There was no evidence of contact with active tuberculosis or any family history of this disease.

Present History.—Onset of arthritis in March, 1950, affecting both hands and wrists. First seen in May, when an apical systolic murmur was also noted. In June a butterfly eruption of acute lupus erythematosus developed on her face. Exacerbation of the arthritis occurred in August. All joints except the hips were hot and swollen. On admission to the Metropolitan Hospital on September 9 her temperature was 99–103° F. (37.2–39.4° C.). Rapid dissemination of the lupus eruption on face, chest, and upper and lower limbs occurred in the next two weeks, associated with increasing anaemia, enlargement of the cervical, axillary, and inguinal lymph nodes, albuminuria, and red-cell haematuria. The apical murmur had become louder, harsh, and prolonged.

Investigations.—*X*-ray film of chest was normal (Special Plate, Fig. 1). The E.C.G. showed normal P waves; low-voltage QRS complexes. Haemoglobin estimation showed levels of 74–50%; white cells 5,000 per c.mm.; E.S.R., 38–75 mm. (Westergren); serum proteins, total 5.3 g. per 100 ml. (albumin 3 g., globulin 2.3 g.). Blood urea, 30 mg. per 100 ml.; blood cultures, sterile. Blood group A, rhesus factor positive; no abnormal agglutinins present. The tuberculin reaction was not obtained, nor was the Hargrave test performed.

On the clinical and laboratory evidence the patient was thought to be a case of acute disseminated lupus erythematosus with probable cardiac manifestations (Libman–Sacks syndrome).

Treatment and Progress

There was no response to salicylates, penicillin, or blood transfusions. On November 14 she was grossly emaciated and toxaemic, and seemed unlikely to live. A.C.T.H. was given for eight to nine weeks, 50 to 200 mg. daily in four divided doses, intramuscularly: total dose, 5,725 g. There was an immediate response, with defervescence, a fall in pulse rate, and loss of pain and stiffness in affected joints. During the next month the swelling of the joints subsided, the rash faded, and the heart murmur became softer. At the onset of therapy fever was controlled completely for three days, and for a further period of one week with increased dosage. Her face became somewhat rounder; she became partially bald, and gained 5 kg. in weight in the first four weeks of treatment. Other signs of adrenal stimulation were an increase in the sodium/potassium ratio and a fall in the circulating eosinophils to zero. The white-cell count showed a lymphopenia; the E.S.R. fell to 16 mm.

From December 24, 1950, to January 3, 1951, there was increasing fever, 99–104° F. (37.2–40° C.). An *x*-ray film of the chest showed increased lung markings in the right cardio-phrenic angle. On January 17 to 19 there was persistent fever 104–105° F. (40–40.6° C.), with considerable general deterioration, but the arthritis and the rash were controlled. An *x*-ray film of the chest showed very numerous miliary deposits in both lung fields, with early confluence of lesions (Fig. 2). The cerebrospinal fluid was normal. A.C.T.H. was stopped and streptomycin, 2 g. daily, begun. This dosage was maintained for one year. It was thereafter gradually decreased, and was stopped finally at the beginning of April, 1952. Auditory acuity began to diminish early in March, 1951, but the clinical evidence of toxicity to the tuberculous process showed no signs of abating. By June she had become stone deaf. Adjuvant P.A.S. was stopped after one month owing to intolerance.

A cold abscess developed in the right forearm in May, 1951. It was drained in July, and was followed by two sinuses, which healed by the beginning of October. At the time of incision this abscess occupied three-quarters of the ventral aspect of the forearm. Three other cold abscesses appeared during August to October: sites, lower end of right sternocleidomastoid muscle, below outer aspect of right knee-joint, and lower third of left thigh.

An *x*-ray film of the chest on November 6 showed miliary infiltrations undergoing calcification (Fig. 3). Her general condition has improved steadily. Temperature and pulse have settled and she has gained 20 kg. in weight since July. The polyarthritis and lupus eruption are still in remission, and the apical murmur has disappeared. The serum proteins totalled 7.6 g. per 100 ml. (albumin 5.1 g.). The systolic murmur disappeared in early February, 1951, at the height of the tuberculous infection, and has not returned. Proteinuria persisted until February, 1952; since then the urine has been clear, and the centrifugalized deposit contains no cells or casts. The remaining cold abscesses have subsided; one has calcified. No tubercle bacilli have been isolated from either sputum or abscesses. The menses, which ceased in September, 1950, returned in December, 1951. The patient started to get up in December, 1951, and was active in the ward from January, 1952, until she went home on April 24 in good health. Streptomycin was administered as (1) the trihydrochloride calcium chloride complex from January to mid-August, 1951, and again from January to April, 1952; (2) dihydrostreptomycin from mid-August to December, 1951.

Recent Investigations.—Serum proteins, total 7.6 g. per 100 ml. (albumin 5.1 g., globulin 2.5 g.); haemoglobin, 86%; white cells, 6,200 per c.mm.; E.S.R., 10 mm. (Westergren); blood urea, 40 mg. per 100 ml. An *x*-ray film of the chest showed dense calcification of miliary lesions. The E.C.G. showed clubbing of P waves.

Comment

There is no doubt that the administration of A.C.T.H. at the time of the acute lupus crisis was life-saving. The immediate response was similar to that reported by other people, but the eventual outcome is unlike any other case of equal severity so far recorded. Over two and a half years have elapsed since the advent of the original illness, and there is now no clinical or laboratory evidence of its activity.

Most people are agreed that acute disseminated lupus erythematosus is an example of a hypersensitivity reaction which in some cases may be associated with a tuberculous infection. However, Klemperer *et al.* (1941) noted the infrequency of arrested tuberculosis and the complete absence of active tuberculosis in 20 consecutive necropsies. Sequeira and Balean (1902) found a tuberculous focus present in 70% of their acute cases, as compared with 18% in their discoid form; but they commented on the rare occurrence of the acute disseminated disease among the large number of patients attending chest hospitals.

In the light of subsequent events it must be assumed that in this case a latent tuberculous focus was present. Whether it was the single sensitizing agent must remain a matter of opinion. It may be argued that the long remission induced by A.C.T.H. and maintained by streptomycin suggests a tuberculous aetiology. But the fundamental changes wrought in the host cannot be explained entirely by the response to a drug whose action is principally on the parasite. Long and Miles (1950) have shown that both A.C.T.H. and cortisone diminish bacterial allergy in guinea-pigs as measured by sensitivity to tuberculin. Rich *et al.* (1950) have found that the incidence of periarteritis and endocarditis produced by intravenous horse-serum injections in rabbits is greatly diminished when cortisone is administered. On the other hand, the known specific effects of these steroids on lymphocytes and fibroblasts may depress the natural resistance of the host.

It is suggested that in this case A.C.T.H. acted both as a non-specific and as a specific desensitizing agent; and that it also induced a profound depression of mesenchymal tissue, as demonstrated by the occurrence of miliary tuberculosis. Nevertheless, a favourable environment appears to have been created for the subsequent action of streptomycin. It may be, as Hart, Long, and Rees (1952) suggest, that the depression of sensitivity and the mechanism of chemotherapeutic action have some common factor.

Summary

A case of miliary tuberculosis in a case of acute disseminated lupus erythematosus is reported.

A possible mode of action by the drugs employed is suggested.

I wish to thank Dr. N. G. Hulbert for his kind permission and encouragement to publish this case, and for so kindly reading the original manuscript; Dr. Raymond Greene for his interest and comments; and the Honorary Editors of the *Proceedings of the Royal Society of Medicine* for allowing me to make use of the preliminary report of November, 1951. I would also like to congratulate the nursing staff of the Metropolitan Hospital, in particular Sister U. J. Young, whose sympathetic handling of the patient contributed so largely to her recovery.

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ERYTHEMA NODOSUM WITH BILATERAL HILAR GLAND ENLARGEMENT

A CLINICAL SYNDROME

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Numerous publications in recent years have thrown new light on the subject of erythema nodosum, and have done much to dispel earlier misconceptions. The view that the condition may occur as a response to a variety of diverse agencies, particularly bacterial and chemical, is now universally accepted. It is found predominantly in children and young adults, and, while primary tuberculosis is the most common cause, acute rheumatism is believed to be seldom associated with it.

As erythema nodosum is so often accompanied by pulmonary changes it should be a routine practice, wherever possible, to make an *x*-ray examination of the chest of all cases, and, if nothing abnormal is found, to repeat the examination a few weeks later. In cases in which there are positive findings subsequent examinations should be made at appropriate intervals until no further information of value is likely to be obtained.

This procedure has naturally led to the discovery of a number of cases of previously unsuspected primary tuberculosis; of more interest has been the discovery of six cases of bilateral hilar gland enlargement with no significant changes in the lung fields. The purpose of this paper is to report this latter group.

Case Reports

Case 1.—Woman aged 26. Developed typical erythema nodosum towards the end of May, 1951. Mantoux 1:100 positive. No chest symptoms. *X*-ray film on July 12 showed enlargement of both hilar and paratracheal glands (Fig. 1). Subsequent examinations showed gradual resolution, and by September 18 the appearances of the chest had returned to normal (Fig. 2).

Case 2.—Woman aged 26. Developed influenza-like illness with erythema nodosum in February, 1949. Mantoux 1:1,000 positive. No chest symptoms. *X*-ray examination

on February 24, 1949, revealed bilateral hilar gland enlargement, especially on the right (Fig. 3). Gradual resolution during following months. On October 26 resolution was not quite complete.

Case 3.—Woman aged 28. Developed erythema nodosum in December, 1949. Mantoux 1:100 positive. No chest symptoms. *X*-ray film on February 9, 1950, showed bilateral hilar gland enlargement (Fig. 4). Chest practically normal on July 5.

Case 4.—Woman aged 28. January, 1950: muscular pains, at first mild, becoming more severe, especially in right gluteal region. March–April, 1950: erythema nodosum with malaise, slight pyrexia, mild aches and pains. Mantoux 1:10,000 negative. (Tests at other strengths were not done.) E.S.R. 60 mm./1 hour (Westergren). On April 11, 1950, there was bilateral hilar gland enlargement (Fig. 5). Tooth extracted on May 2 for apical abscess: culture gave heavy growth of *Streptococcus viridans*. September, 1950: tonsillectomy; culture, *Str. viridans*. Resolution complete on September 28.

Case 5.—Woman aged 37. Typical case of erythema nodosum in May, 1951. The *X*-ray appearances of the chest and subsequent progress were exactly like those of the above cases.

Case 6.—Woman aged 27. Admitted to hospital on February 24, 1950, with a history of pain in wrists, elbows, knees, and ankles of 10 days' duration. Erythema nodosum on legs for several days. Sore throat (history of recurrent sore throats). Throat swab at time of admission contained mixed flora with heavy growth of haemolytic streptococci. Mantoux test (March 8, 1952) 1:10,000 positive. *X*-ray film on admission showed bilateral hilar gland enlargement; subsequent examinations showed gradual return to normal.

(Since this paper was written we have seen three further cases of erythema nodosum in adults—one with bilateral and two with unilateral hilar gland enlargement.)

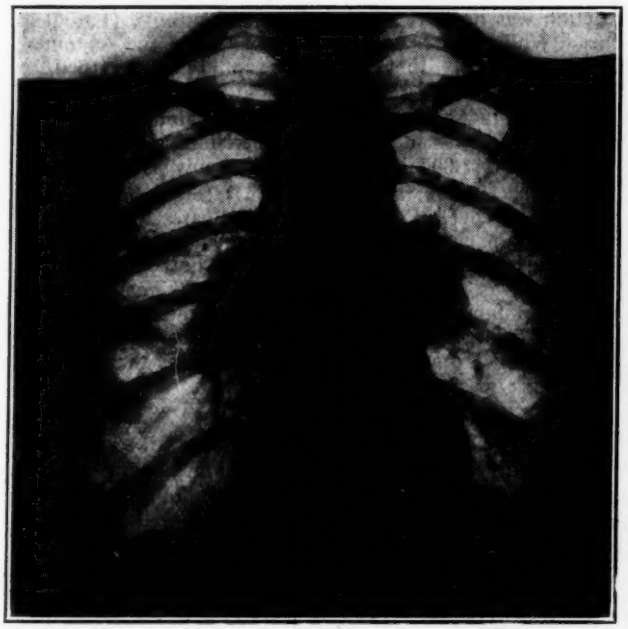

FIG. 1.—Case 1. Radiograph taken on July 12, 1951, showing enlargement of both hilar and paratracheal glands.

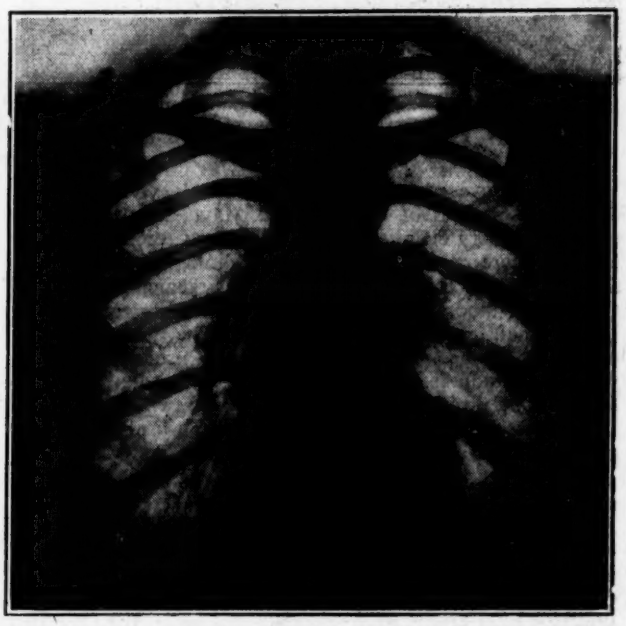

FIG. 2.—Case 1. Radiograph taken on September 18, showing return to normal.

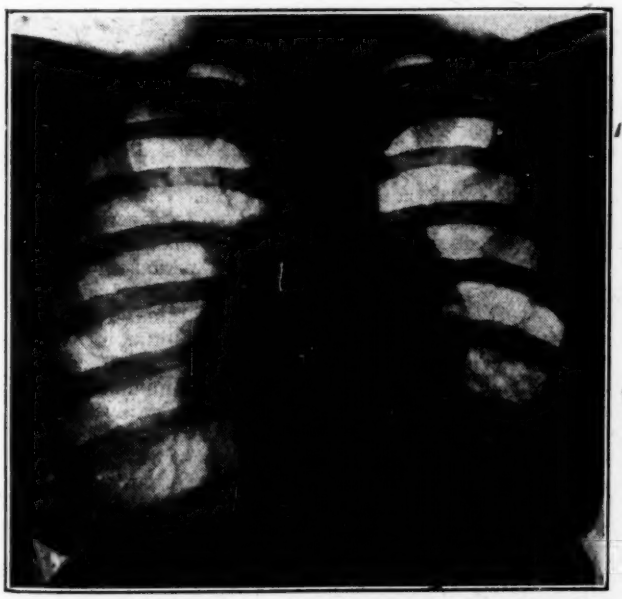

FIG. 3.—Case 2. Enlargement of hilar glands, especially on the right.

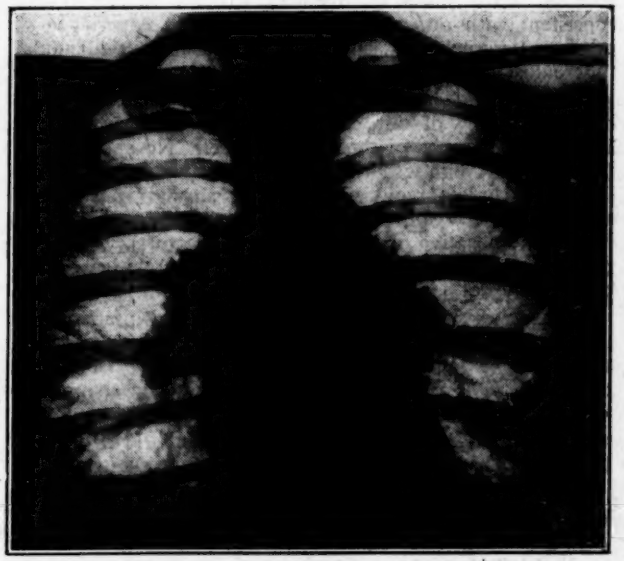

FIG. 4.—Case 3. Bilateral hilar gland enlargement.

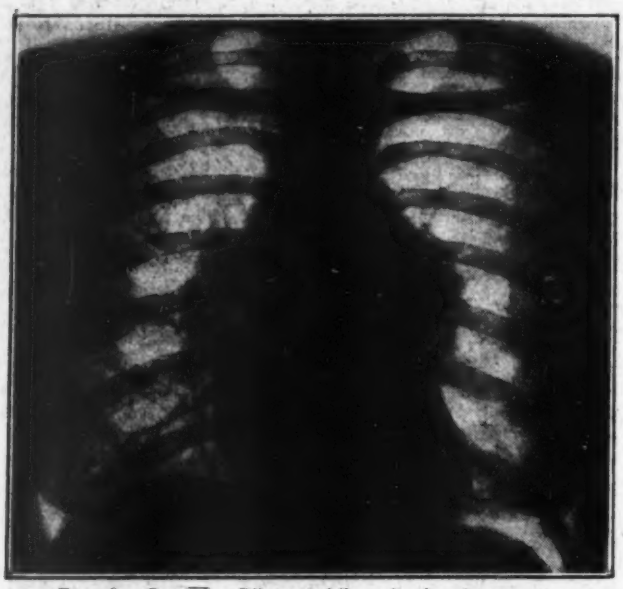

FIG. 5.—Case 4. Bilateral hilar gland enlargement.

Discussion

All the above cases occurred in relatively young women during the months of December to May. In none of the cases were there definite signs or symptoms referable to the lungs. There were no significant radiological changes in the lungs apart from the glandular enlargement. No case showed peripheral glandular enlargement or any other visceral manifestations of significance. The time of resolution varied to some extent, but it was usually complete within six months. In five cases the Mantoux test was found to be positive, and in one case negative at 1:10,000. Unfortunately, as the patients were almost all at home, more detailed examinations were not possible.

It seems probable that cases of this nature represent a special syndrome; the aetiology is uncertain. In all likelihood there were, during the period in question, further cases of a similar nature in Hull and district of which we were unaware. The total number of such cases throughout the country may therefore be quite considerable, and it is hoped that this brief report may stimulate interest in the problem.

In relation to the aetiological possibilities one must consider the known causes of erythema nodosum.

Tuberculosis.—Primary complex can be excluded, as bilateral hilar gland enlargement of this nature is not consistent with our present conception and experience of primary tuberculosis. The relatively rare adult glandular tuberculosis is unlikely for similar reasons.

Sarcoidosis.—There was no clinical evidence of sarcoidosis in any of our cases, and no bone changes were seen in radiographs of the hands or feet. No special tests, such as the Kveim test, were done. Positive tuberculin tests do not exclude sarcoidosis, though a strongly positive reaction is rather against such a diagnosis (cases of sarcoidosis tend to be negative or weakly positive reactors). The complete resolution of the lesions in such a relatively short time, while not excluding sarcoidosis, is not in favour of it.

Bacterial or Virus Infection.—Streptococcal infections are regarded as being an occasional cause of erythema nodosum, and it seems quite possible that these cases, from their nature, may be related to some bacterial or perhaps virus infection. There is, as yet, no definite confirmation of this.

Sulphonamides or Other Chemical Agents.—No drugs of this nature had been given in any of these cases.

What is the relationship of our cases to similar cases previously reported? Kerley (1943), discussing the aetiology of erythema nodosum based on a study of the disease in 37 adults with an average age of 21, found eight cases with enlarged bronchial glands and without pulmonary changes. It seems probable that some of these eight cases are similar to ours, although this group is not discussed in detail. He believes that in some cases the radiological appearances are identical with those described in sarcoidosis.

Middlemiss (1949), reporting on 124 cases, found 56 with pulmonary changes, only one of which bears any possible relationship to ours. He regards his case as non-tuberculous, although the Mantoux reaction was strongly positive at 1:10,000.

Sterling (1950) reports two cases of erythema nodosum with bilateral hilar gland enlargement, the *x*-ray appearances being, so far as can be determined, identical with our cases. In both instances the Mantoux reaction in all strengths was negative. The serum of each patient was found to possess tuberculin-neutralizing properties. In spite of this he concludes that a diagnosis of sarcoidosis is not justified. He suggests that this is a peculiar clinical syndrome which merits further investigation.

Crawley (1950) discusses three cases of erythema nodosum with bilateral hilar gland enlargement. The Mantoux reaction was negative in two cases, and positive (1:100) in one. While no histological proof could be obtained, Crawley suggests that his cases could be regarded as sarcoidosis.

Löfgren (1946) regards his cases of bilateral hilar gland enlargement, with a negative tuberculin reaction or a reaction of 1:1,000 or 1:100, as probably sarcoidosis.

Johnson, Hanson, and Good (1951) found hilar adenopathy in 9 out of 100 consecutive cases of erythema nodosum; in eight of them the adenopathy was bilateral. They suggest that hilar adenopathy has not been generally recognized as an accompaniment of erythema nodosum. Follow-up films of five patients were available; in three the hilar enlargement had disappeared in from one to seven months. They draw no conclusions regarding the aetiology.

Summary

Six cases of erythema nodosum are described in young adults with bilateral hilar gland enlargement and no other pulmonary changes; the possible aetiology is discussed. The condition seems to warrant the title of a clinical syndrome, and collation of further similar cases is desirable.

We wish to express our indebtedness to Dr. N. Gebbie, formerly M.O.H., Hull, and to those general practitioners who were kind enough to assist us in investigating their cases.

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Fulbright travel grants are again offered to citizens of the United Kingdom and Colonies to go to America for an academic or educational purpose. Applicants must guarantee financial support in dollars for their period of stay in America. Graduate students must show proof of admission to an American institution of higher learning. All applicants must be affiliated with such an institution. In the case of medical internships, the hospital concerned must be associated with a medical school. The minimum period of study in the U.S. for graduate students is nine months. Professors, lecturers, and senior research workers must intend to stay at least three months, of which about two-thirds should be at one university. The awards are competitive and there are two closing dates, March 16, 1953, for those travelling between June 1 and July 31, 1953; and June 15, 1953, for those travelling after August 1, 1953. Applications should be sent to the United States Educational Commission in the United Kingdom, 55, Upper Brook Street, London, W.1.

Medical Memoranda

Microsporosis due to M. Canis in Schoolchildren and Domestic Animals

In spite of improved standards in hygiene and public health in modern times microsporosis among schoolchildren still occurs often enough to be a cause for anxiety to both public health and educational authorities. In some districts a periodic check-up on children attending school or living in institutions is sufficient to control its spread; in others such measures applied only to children are not sufficient. The reason for this is that one species of *Microsporum, M. audouini,* is carried by children only, whereas the other species, *M. canis,* is commonly carried by cats and dogs as well. Walker (1950) illustrated this in her distribution map for microsporosis in Great Britain and Northern Ireland for the years 1946–9 inclusive, which shows cities and towns where one species of *Microsporum* predominated or sometimes occurred to the exclusion of the other. For instance, in Huddersfield, strains of *M. audouini* only, whereas in Barnstaple strains of *M. canis* only, were isolated.

Experience in Leeds

In 1950 in Leeds, where *M. canis* strains have in recent years been overwhelmingly predominant as the aetiological agents of tinea capitis and tinea glabrosa, a campaign was started to stamp out ringworm in the schools, and this is still in progress. In this campaign the departments of public health, the school medical authorities, and the staff of the dermatological department of the Leeds General Infirmary have joined forces, and already some measure of success appears to have been achieved, if one may be permitted at this early stage to interpret the figures published by the school medical officer of health, Dr. I. G. Davies, in his annual report for 1951, as indicating progress. Thus for scalp ringworm only, he gives the following figures for the last three years for the City of Leeds: 1949, 56; 1950, 43; 1951, 18. With only a few exceptions these figures refer to schoolchildren with microsporosis due to *M. canis.*

The routine procedure adopted in Leeds is briefly as follows. All schoolchildren who are diagnosed at the school clinic as suffering from tinea capitis or tinea glabrosa, or both, are sent on to the department of dermatology of the Leeds General Infirmary for further investigation. Here they are carefully screened with Wood's lamp and by microscopical investigation; specimens are also collected for culture. If the result of these examinations is positive the children concerned are debarred from attending school until clear of infection. If it is ascertained that a cat or dog (or both) is kept in the home of the patient, contact is made immediately with the staff of the city's disinfestation centre, who collect the animals concerned as soon as possible, examine them with the aid of Wood's lamp, and convey all positive or doubtfully positive animals to me. If infection is confirmed they are then kept for further investigations, which include the culture and typing of the fungus causing the infection, and are not returned to their owners until clear of infection.

During 1950 and 1951 some 138 Leeds patients, including children under school age and a few adults, have attended the skin clinics with microsporosis due to *M. canis,* but in only a small proportion of these was it possible to trace the infection to its animal source. Altogether, in the City of Leeds, only nine infected cats, including kittens, and six infected dogs, including puppies, were collected during this period. Even taking into account the spread of infection in families and schools among children it is evident from these figures that many infected cats and dogs are still at large and are forming a reservoir of infection.

With regard to microsporosis in cats due to *M. canis,* an interesting though somewhat disturbing fact is that a high proportion of the infected cats (especially the kittens) collected in Leeds and the outlying districts (26 out of 30 so far examined) have presented no superficial lesions of the skin proper, or else the lesions have been detected only on close examination. This means, of course, that it is only when the cats or kittens belonging to patients with microsporosis are examined that these otherwise unsuspected cases of feline microsporosis are discovered.

Comment

It has been customary to associate the incidence of ringworm with unhygienic habits or surroundings, and a certain social stigma rightly or wrongly attaches to it, but if infected cats with no visible signs of their microsporosis roam the streets any child is liable to contamination or possible infection. The introduction of measures of control more extensive even than those which are being practised in Leeds would therefore seem to be necessary in order to protect the public adequately from possible infection by cats affected with this disease.

My thanks are due to Dr. J. T. Ingram and Dr. I. G. Davies for encouragement and co-operation, and to all those who have participated with me in this work.

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Haematoma of the Umbilical Cord

The literature on this rare condition has been reviewed by Dippel (1940) and Browne (1950). According to Dippel, the occurrence is 1 in 5,505 deliveries at or near term. Half the infants in such cases are stillborn—frequently a macerated infant being delivered. It is suggested that in most cases the haematoma forms before labour or during delivery.

Case Report

The mother, a 3-gravida, had had an uneventful pregnancy. The Wassermann reaction was negative, and there was no evidence of toxaemia. A caesarean section was performed at term as the mother had recently had a pelvic floor repair. A living female infant, weighing 8 lb. 2 oz. (3.7 kg.), was delivered without difficulty. Two clamps were applied to the cord 2 in. (5 cm.) apart and 9 in. (22.8 cm.) from the umbilicus, and the cord was divided between the clamps.

The infant cried lustily at birth and was placed in a cot. An hour later, when she was about to be bathed, a soft, dark-blue, fluctuant swelling had appeared in the umbilical cord. It was 2½ in. (6.3 cm.) long and 3 in. (7.6 cm.) in circumference, and extended up to the umbilicus, where it ended abruptly. A ligature was tied round the cord immediately distal to the swelling in the hope that this would prevent any extension. The remainder of the cord was cut and spirit dressings were applied to the stump and round the swelling.

The next day the swelling had diminished slightly and was hard and black. It remained in this condition until separation took place on the eleventh day, leaving an entirely normal umbilicus.

Comment

The following are stated in the literature to be a cause of the condition: (1) rupture of one of the vessels of the cord—whether arterial, venous, or capillary; (2) diapedesis of red cells following obstruction to the cord.

It is suggested that the condition may be caused by congenital thinning of the vessels, degenerative changes in the vessel walls, varicosities of the vein, thrombosis in the vein, decreased resistance of the vein wall due to icterus, or trauma. The aetiology in this particular case is obscure unless it be that there was some congenital weakness in a vessel wall, or that clamping of the cord caused rupture.

My thanks are due to Mr. P. R. Mitchell for permission to publish this case, and for his encouragement and advice.

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Late House-Physician, Maternity Department,
Royal Hants County Hospital, Winchester.

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Reviews

CLASSIFICATION OF DISEASES

Textbook and Guide to the Standard Nomenclature of Diseases and Operations. By Edward T. Thompson, M.D., F.A.C.H.A., and Adaline C. Hayden, R.R.L. (Pp. 620. $8.) Chicago: Physicians' Record Company. 1952.

This book is designed to help medical records officers in hospitals where the *Standard Nomenclature of Diseases and Operations* is used or where a record system is to be installed based upon it. It contains much information about changes in the new fourth edition of the *Nomenclature* and explains how to combine its use for internal record-keeping with use of the *International Statistical Classification of Diseases* for presentation of statistics.

The first four chapters of Part I deal generally with the history, structure, and application of the *Standard Nomenclature*; and three disease systems which have undergone considerable revision in the fourth edition are then discussed in some detail—namely, the so-called "psychobiologic unit," the haemic and lymphatic systems, and neoplasms. For some of the changes made, such as that from myeloid to granulocytic leukaemia, world-wide adoption is likely to be somewhat tardy, since the new designation does not appear even in the index of the *Nomenclature of the Royal College of Physicians.* The next chapter explains how to install a recording system based on the *Standard Nomenclature.*

The clear exposition of the relationship between the *Standard Nomenclature* and the *International Statistical Classification* in the ninth chapter should help to remove a good deal of misunderstanding. It is summed up in the statement that "it is obvious to those who have utilized both systems that they are not antagonistic but complementary. Each has specific purposes to fulfil and each is interdependent upon the other." A full description follows of the *International Classification* itself and of the method by which, in the fourth edition of the *Standard Nomenclature,* each clinical condition has not only its standard code number but also, in parentheses, the international category to which it belongs.

This correlation between the two codes was carried out by the revisers of the *Standard Nomenclature* with great care and will be of incalculable assistance to the World Health Organization in correcting and revising the international classification in due course. It is regrettable that in their enthusiasm for correlating the two codes the editors of the *Standard Nomenclature* invented numerical subdivisions for some international categories, thereby violating an important recommendation of W.H.O. (set out on page xxxiii of Volume I of the *Classification*). This is: "If such subdivisions are created, it is recommended that letters instead of numbers be employed, especially in publication, to indicate that the item is not a part of the international classification." Failure to observe that request in a publication so important as the *Standard Nomenclature* creates difficulties for W.H.O. in making future subdivisions of their categories by international agreement, and makes it difficult for anyone to know which subdivisions are international and which not. Indeed, the position has already arisen that one series of subdivisions of a category of malignant neoplasms (No. 199) has been recommended by an Expert Committee of W.H.O, and endorsed by the World Health Assembly, while another series, designated by the same digits, has been printed in the fourth edition of the *Standard Nomenclature.* For this state of affairs the editors of the *Textbook and Guide* are not responsible; and indeed they say very wisely (of the Standard Code) that "those who change the terminology prior to approval of the change by the appropriate sponsoring association are regressing to the conditions which existed before the establishment of the *Standard Nomenclature*" (p. 183). This applies with even greater force to arbitrary addition of numbers to the international code.

Chapter 10 explains how to install the *International Classification* in an institution already using the *Standard Nomenclature,* and how to install both systems of recording simultaneously. The last four chapters of Part I discuss possible modifications and elaborations of the *Nomenclature* code and special problems and difficulties arising in its application.

The second part is devoted to a classification of diagnoses according to the clinical service of a hospital most likely to deal with each. Four major services—medicine, surgery, obstetrics, and newborn—with eight or nine subdivisions of the first two, are denoted by letters, and an alphabetical list of diagnoses assigns to each the appropriate service letters. It is difficult to understand how hospital clerks using this index can be expected to know, for example, that when they fail to find carcinoma or malignant neoplasm of the breast or other organ in the index they must look for adenocarcinoma under A, where 37 separate sites will be found listed. The inclusion in the book of 250 pages whose value is problematical was a mistake, in the reviewer's opinion. But Part I will be indispensable to the medical records officer who is using the fourth edition of the *Standard Nomenclature* and who takes his specialty seriously.

PERCY STOCKS.

THE ROYAL MEDICAL SOCIETY

History of the Royal Medical Society, 1737–1937. By James Gray, M.A., F.R.S.Ed. Edited by Douglas Guthrie, M.D., F.R.C.S.Ed. With foreword by Sir Robert Hutchison, Bart., M.D., LL.D., F.R.C.P. (Pp. 355. £2 2s.) Edinburgh: University Press. 1952.

The story of the development of the Medical School of Edinburgh and of the men who were trained there provides an epitome of the history of medical education in this country and thoughout the English-speaking world, since from Edinburgh its graduates have gone forth to London and the rest of England, to the Dominions and Colonies, and to America, and played leading parts in founding and developing their schools of medicine. It was but a few years after the Faculty of Medicine was founded in the University of Edinburgh in 1720 that the Medical Society was formed, which later obtained a Charter from George III. This Society is unique, for it is the oldest medical society in the country and its active members are students and young graduates.

The author of this book, though not himself a doctor, was connected with the profession and deeply interested in the Society. He gives brief biographies of the remarkably many members who subsequently achieved fame, and has paid particular attention to their influence on the University of Edinburgh and the many universities throughout the world where they found their life's work. The story of the Society is in this way a source of valuable information on the history of medical education, but it is also a human document showing how youth acquires responsibility by being left to manage an ancient and royal society. Probably this influence on its members has been more valuable than the addresses by eminent guests and its scientific papers. From the records and minutes of its meetings, Gray might have produced a valuable but dull account of this important institution, but this is a very readable book, full of human affairs which will interest many who have had no personal connexion with Edinburgh or its Royal Medical Society.

FRANCIS FRASER.

THE SCALP

The Scalp in Health and Disease. By Howard T. Behrman, A.B., M.D. (Pp. 566: 312 illustrations. £4 15s.) London: Henry Kimpton. 1952.

This is a well-balanced and well-produced book which demands little but praise from a reviewer. It is likely rapidly to take its place as a standard work, and therefore can

be recommended to all who require a monograph on the subject with which it is concerned. The opening chapter is on embryology, anatomy, and physiology. It contains much that is of interest, and to write it the author must have spent many hours reading and assessing a wide variety of essays scattered in many journals and books. The second chapter is concerned with normal scalp, "hair dressing," and—in significant juxtaposition—"dermatitis." Behrman has avoided the pitfall of making this section too long, and has constructed a brief, authoritative, but adequate survey of the subject.

The remaining chapters are concerned with alopecia, seborrhoeic diatheses, infections, psychogenic disorders, maladies due to involvement of the scalp by systemic and cutaneous diseases, and tumours. At the end of the book there is an appendix containing many formulae and a satisfactory index.

M. B. Sulzberger has contributed a foreword. "I cannot say," he writes, "that I agree with every word in this book . . . there are quite a few statements which allow for honest differences of opinion. . . ." The present reviewer finds himself in warm agreement with these remarks. Particularly, to take but one example, he finds it difficult to accept a system of classification which does not include familial premature alopecia of males as a separate entity but includes the condition in an omnibus title "male pattern alopecia (common baldness)." Other readers may well take exception to the author's action in including alopecia areata as a "scalp disorder of psychogenic origin (proved or presumptive)." Behrman may well be correct, but most logicians could easily demolish the arguments which have been advanced by many authors in support of this theory of aetiology. These, however, are but "honest differences of opinion," and those who read the book carefully will find others on which to sharpen their critical faculties. But in general they will probably agree that this is both an admirable and a useful book.

R. M. B. MACKENNA.

YAWS

Bone Lesions of Yaws in Uganda. By C. J. Hackett, M.D., F.R.C.P. (Pp. 194; 133 figures. £2 5s.) Oxford: Blackwell Scientific Publications. 1952.

This book, by an acknowledged authority, is based on a detailed study of some hundreds of cases of yaws with bone lesions in Lango in the Protectorate of Uganda. The author begins with an introduction detailing geographical and technical information, and giving a very brief account of the Lango tribe. Sections follow on the aetiology of bone lesions observed in radiography and clinical descriptions of the bone lesions observed in each stage of the disease. The book ends with a summary in which there is an all-too-brief discussion on the bone lesions of yaws and syphilis, which concludes with the bleak words, "It may be said that apart from the absence of osteo-chondritis in yaws, there are probably no bone lesions that occur in one disease that may not be observed in the other."

The classification of yaws lesions was based on the skin changes observed. Lesions were grouped as primary or secondary, in both of which the treponemata could usually be readily demonstrated, and tertiary, in which treponemata were rarely found. Secondary generalized lesions were never destructive, and healed with insignificant scars. Tertiary lesions were characterized by destructive ulceration which healed with atrophic scars. Tertiary lesions appeared later in the disease and were never present contemporaneously with secondary lesions; the latter never appeared after the development of tertiary lesions.

Bone lesions appearing contemporaneously with secondary skin lesions were regarded as secondary. A late secondary stage is described to include bone changes resembling secondary lesions, but occurring in the absence of skin lesions. Tertiary bone lesions were "first recognized by their incidence in patients with typical tertiary skin lesions. Cases with no skin lesions but with bone lesions resembling those in the tertiary cases were included in the tertiary group; in some of these tertiary skin lesions subsequently developed."

Secondary bone lesions usually developed during an eruption of skin yaws. The majority appeared in children of 5 years and under. The affected regions were tender and swollen. The pathological processes included rarefaction of the bone cortex and periosteal deposits. Resolution resulted in cortical thickening and bony expansion. Further activity or resolution sometimes followed. In general, numerous bones (especially when the hand or foot was concerned) were involved in the secondary changes. Ulceration to the surface and spontaneous fracture did not occur in this stage. The author summarizes the secondary changes as "a non-suppurative inflammatory reaction of the various tissues of bone." He considers that there is no evidence that yaws played any part in "bowing" of the tibial shaft.

Tertiary lesions occurred in older patients, the majority being over 10 years of age. There was usually some localized bony swelling and pain. The active processes consisted in focal rarefactions, usually well defined and sometimes multiple, in the thickened cortex of expanded bone. Ulceration through the skin and spontaneous fracture sometimes occurred. Resolution was slow, and the destructive nature of the lesions was usually evident. The author considers gangosa "a characteristic destructive tertiary yaws lesion."

The book contains a great deal of interesting, detailed information and is undoubtedly a major contribution to tropical medicine. The great pity is that its text is so carefully confined to the title subject. The author's great knowledge of other aspects of the disease is only glimpsed. It is to be hoped he will one day widen the view into a study of yaws as a whole. The author and the publisher are to be congratulated on a fine book.

B. G. MAEGRAITH.

CLOT RETRACTION

Clot Retraction. By O. E. Budtz-Olsen, M.D. (Pp. 149; illustrated. £1 5s.) Oxford: Blackwell Scientific Publications. 1952.

The subject of clot retraction is essentially one for the specialist in haematology. It presents many interesting and varied aspects, which are most ably discussed and analysed by Dr. Budtz-Olsen. This monograph consists of a detailed review of the theories and practical applications of the subject, and the author has, in a masterly manner, reinforced the theoretical structure, where he has found it weak, with new and original experiments of his own. He fully discusses all the usual techniques used for measuring clot retraction and points out the factors which may modify results at the laboratory bench, elucidating them by figures obtained from personal observation. Such subjects as the influence of vessel shape, temperature, the importance of formed blood elements, and the effects of the various plasma-clotting factors are dealt with in this manner. Wherever helpful, line diagrams and photographs have been included in the text, and the general production and printing of the book are satisfactory.

This monograph will be of interest to all engaged on problems of blood coagulation. It offers in small bulk a review of over 400 original papers in many languages, and for the bibliography alone we should be deeply grateful. The book fails perhaps in one respect only: the author's own views on certain points are not clearly expressed. He says, as it were, Here is the evidence, draw your own conclusions. This, in fact, is often the main difficulty even to those who are thoroughly conversant with the problems of clot retraction.

H. PAYLING WRIGHT.

BRITISH MEDICAL JOURNAL
LONDON
SATURDAY NOVEMBER 15 1952

HEALTH AND LOCAL GOVERNMENT

The pattern of health administration has a tendency to repeat itself, and in this country we do not seem to learn by trial and error. Less than 100 years ago there were no health services as such but a chaos of authorities, often in conflict with one another. During the last quarter of the nineteenth century a brave attempt was made by legislation to bring about some degree of order: the tidy arrangement of county boroughs, and of counties with their brood of small boroughs and urban and rural districts, gave a new impetus to local government and greatly strengthened the electoral principle. The system was far from perfect, because the poor-law system remained parallel and independent. There were other anomalies, but it seemed clear that a great advance had been made towards a coherent scheme of local government. Unhappily the national health insurance plan of 1911 set up fresh obstructions by abandoning local government and the electoral principle; and the decision was all the more tragic because it was determined by a justifiable dislike of the Local Government Board and of its president, John Burns. The creation of a new *ad hoc* authority for medical care was itself a cause of cleavage between general medical practice and the local health authorities. Indeed, the position of tuberculosis—a service poised uneasily between the two—was so awkward that the service had to be transferred after the war to the major local authorities.

The year 1929 marked a splendid new attempt to co-ordinate local authority services. Under the Local Government Act of that year the boards of guardians, including their hospitals, were absorbed by the county and county borough councils; and in the following year notable improvements were made in the mental hospital services. It seemed once again as if the road was clear for further co-ordination: a definite direction had been given for the break-up of the poor law, and progressive steps were ready to be taken, in the interests of efficiency and financial stability, to enlarge the areas of local government without destroying either the electoral principle or "the sentiment which in this country has always tended to grow most easily and to strike the deepest roots in attachment to the conduct of affairs within the narrowest possible limits."[1] During the decade that followed, notable progress was in fact made towards the co-ordination of the hospital system with local public agencies, and the combination of voluntary insurance plans with financial support from local authorities might well have saved the voluntary hospital system.

This structure was heavily damaged in the second world war, but the position offered great opportunities for reconstruction to maintain the electoral principle while securing larger and more efficient areas of local government. These chances were unfortunately thrown away at the end of the war through two principal errors: the failure to make the reform of local government a primary task of reconstruction, and the abandonment of the system of popular election by the creation of *ad hoc* regional authorities for the control of hospitals. The effect of this policy of expediency was to perpetuate in the field of medical care three independent authorities: the hospitals, under appointed regional boards with areas far too large to maintain local interest; general medical practice, under executive councils; and the old, unregenerate local authorities to deal with the rump of the public health services.

In an address—delivered at the Annual Meeting of the B.M.A. in Dublin and published in last week's *Journal* (p. 1007)—on the future of the local authority health services Professor Leslie Banks referred to the multiplicity of organizations now dealing with our medical services, and he asked whether local authorities should retain any health services at all. "Why not make an all-purpose health and hospital region?" he suggested. This would indeed be a more effective step towards unity than the recent recommendation that the untidy parcel should be tied up by local joint consultative committees. In a democracy such as ours, however, two criteria must be satisfied: the first is that the all-purpose bodies should be elected by the people living in the area served; and the second that the regions should be small enough to retain local interest and local pride in its institutions. As Banks says:

"A regional authority administering health and hospital services, including perhaps industrial medical services, could soon become the object of attack from two opposite sources. The central government departments might regard such an authority with great distrust and do all in their power to curb its growth. The people in the area served would . . . soon protest against remote control and 'dictatorship.'"

1 General Circular to Local Government Act, 1929.
2 *Interim Report on the Future Provision of Medical and Allied Services.* 1920. H.M.S.O., London.

In considering the future of local authority health services Banks begins by posing what he regards as one fundamental question:

"Do we still believe that the prevention and cure of disease are distinct entities to be retained in separate administrative and technical compartments? If we do, then not only must the distinction between local authority and hospital and general-practitioner services be maintained but other new services, such as an industrial medical service, must be established and two kinds of worker, preventive and curative, must be trained. I suggest that the distinction is no longer tenable, and that prevention, diagnosis, treatment, and aftercare now form one continuous process and that we should revise our undergraduate and postgraduate teaching accordingly."

This was also the gist of the comments in the Dawson report[2] of 1920, and one of its principal suggestions was that the general practitioner should be trained in both prevention and treatment. This is still the answer to the present problem, and Banks's suggestion that the time has come to merge the maternal and infant welfare services with the hospital and paediatric services amounts to the exclusion of the family doctor. It is surely in the family rather than in the hospital that prevention and medical care should be conjoined.

Another difficulty in the logic of Banks's argument is that he appears to use the word "prevention" in the restricted sense of prevention of disease. He is quite entitled to do this, so long as he makes it clear that this limitation by no means applies to the work of local authorities and their medical officers. One of the main functions of these bodies is to promote health, and a primary interest of their medical staff, in schools and maternal and child welfare centres alike, is to give guidance to well mothers and their children, and to encourage, train, and comfort the healthy expectant mother. Much of this important work is best carried out by group teaching, and it is to be hoped that family doctors will take their full share in this—but it would be a mistake to make the hospitals the centres for such teaching.

ERYTHROMYCIN

Of the "broad spectrum" antibiotics derived from soil streptomyces, chloramphenicol and aureomycin appeared in 1948 and terramycin in 1950. Assuming that any further such substances exist, the discovery of another was due, and it has duly appeared after a two-year interval. This is "erythromycin" (also named "ilotycin"), obtained from a strain of *Streptomyces erythreus* found in a soil sample from a small island in the Philippines. McGuire and his colleagues[1] of the Lilly Research Laboratories announce its discovery and describe its physical and chemical properties and antibacterial activity. Heilman, Herrell, and Wellman[2] give a general account of the behaviour of the new drug *in vitro*, and of the effects of its use in various patients in the Mayo Clinic, and Haight and Finland[3] describe a similar study at the Boston City Hospital.

Erythromycin is a basic substance, soluble in water to the extent of 2 mg. per ml., reasonably stable, and much more active in an alkaline than an acid medium. It has a bactericidal as well as bacteriostatic action: bacteria can acquire resistance to it—apparently with some rapidity—but this resistance is unrelated to that to any other antibiotic. Its "spectrum" resembles that of penicillin, Gram-positive organisms and a few of the more fastidious Gram-negative (*Neisseria* and *Haemophilus*) being sensitive, and coliform bacilli resistant. As with penicillin, haemolytic streptococci are highly sensitive and staphylococci rather less so: on the other hand, corynebacteria are exceptionally sensitive to erythromycin, and it is of some significance that Haight and Finland have cleared three persistent diphtheria carriers with it. The drug is administered by the mouth and behaves pharmacologically like the other newer antibiotics: therapeutic concentrations can easily be maintained in the blood, but at the same time, whether owing to incomplete absorption or to biliary excretion, there is a pronounced effect on the faecal flora, Gram-positive elements including clostridia being suppressed and coliforms unaffected. Daily dosage has varied from 1 to 3 g. and dosage intervals from 3 to 6 hours. The only factor limiting dosage is a tendency of the drug to cause vomiting and diarrhoea, no other toxic effect having been seen. Therapeutic results in pneumonia and in streptococcal throat infections have been as good as those obtainable with other antibiotics. A more important use for erythromycin is suggested by the successful treatment of two cases of staphylococcal septicaemia (one in each series) in which the organism was resistant to other antibiotics. On the other hand, failure in four out of five cases of endocarditis suggests that the capacity of bacteria to acquire resistance to this drug may intervene here: such a change was actually demonstrated in two of these cases.

First impressions are that erythromycin will be a valuable agent to hold in reserve for infections resistant to everything else. The general tendency among staphylococci and coliform bacilli to become resistant to the newer antibiotics as well as the old is illus-

[1] *Antibiot. and Chemother.*, 1952, **2**, 281.
[2] *Proc. Mayo Clin.*, 1952, **27**, 285.
[3] *New Engl. J. Med.*, 1952, **247**, 227.
[4] *Med. J. Aust.*, 1952, **1**, 870.
[5] *Antibiot. and Chemother.*, 1952, **2**, 279.

trated in the findings of Thomson,[4] who mentions incidentally that three patients at the Royal Prince Alfred Hospital, Sydney—two with pneumonia and one with septicaemia resulting from cross-infection with a totally resistant staphylococcus—all died. This gradual process of bacterial habituation to drugs during the years following their discovery makes it all the more necessary for fresh ones to be forthcoming at intervals, and it is reassuring to know that we have not reached the end of Nature's resources in this direction.

A leading article[5] in the journal containing the first announcement of this discovery mentions some interesting facts. It is well known that several firms in the U.S.A. are conducting extensive soil-screening programmes with samples from all over the world with a view to discovering new antibiotic-forming species. Erythromycin is, of course, the product of such a survey, and Eli Lilly & Co. are now added to the list of those fortunate concerns who have discovered a winner. But it is here stated that the number of firms engaged in such screening programmes is 16. Although the extent of these operations and the skill with which they are conducted are important, chance is perhaps still more so; a lucky dip on such a scale has never been seen before in anything connected with medical science. It is also mentioned that the monthly American production of penicillin is now 30 tons, of streptomycin 21, of aureomycin, chloramphenicol, and terramycin 24, while that of sulphonamides is, surprisingly enough, on the upgrade also. It would be interesting to know what proportions of these vast quantities of antibiotics (enough to supply a 10-g. course to over 90,000,000 patients annually) are being used for necessary purposes.

CHLOROPHYLL

The sale of chlorophyll preparations in the United States is now enormous, and the increasing demand has astonished even those who sell them. One reason for this is the interest taken throughout North America in the use of drugs and disinfectants which may improve health. A second factor which has played a great part in accounting for the large sale of chlorophyll preparations is television. In many parts of the United States television sets are in nearly every home, and the firms selling chlorophyll preparations have made the fullest use of this medium to advertise their wares. Young men and young women appear on the screen to explain that "you must have a nice breath, I don't mean just for kissing," and that this is possible if you chew chlorophyll tablets or use tooth-paste containing chlorophyll or take chlorophyll in one way or another. This advertising has succeeded beyond all expectation. That it should have done so in the United States is the more surprising, where an understanding of scientific observations seems more widespread than in Britain. Many Americans must surely know that, in chewing six chlorophyll tablets each containing 100 mg., they are taking no more chlorophyll than is present in a fraction of an ounce of cabbage or other greenstuff.

That is one side of the picture. What is the other? In the first place evidence has been obtained that chlorophyll dressings reduce foul odours associated with wounds. This appears in so reliable a setting as a report to the Council on Pharmacy and Chemistry of the American Medical Association published in 1949.[1] The evidence was principally the general impressions of the staff and patients of surgical units; a few tests were made in which, for example, three to six independent observers were asked to classify the wounds in four grades according to smell. Gruskin,[2] who used his own patented "substantially pure water-soluble chlorophyll" in isotonic saline or in a lanoline ointment, stated that it was effective in reducing odour in over 1,200 cases of suppurative infection, mostly of ear, nose, and throat. The cases were not described. Goodman[3] found that application of 60 mg. of chlorophyll powder with 300 mg. of activated charcoal or kaolin reduced the odour of colostomy more than did the adsorbents alone.

It has been suggested that the reduction of odour in these cases is due to bacteriostatic action. L. W. Smith[4] found that *Pseudomonas pyocyanea* failed to grow or to survive in the presence of water-soluble chlorophylls. He considered that chlorophyll acted as an oxidizing agent which made the medium unfavourable for anaerobic growth. That is at least a rational suggestion. Bowers,[5] on the other hand, believed that the most important effect was stimulation of the tissue. In nasal infections the effect was too rapid to be accounted for by bacteriostasis or by

[1] Moss, N. H., Morrow, B. A., Long, R. C., and Ravdin, I. S., *J. Amer. med. Ass.*, 1949, **140**, 1336.
[2] *Amer. J. Surg.*, 1940, **49**, 49.
[3] *Surgery*, 1950, **28**, 550.
[4] *Amer. J. med. Sci.*, 1944, **207**, 647.
[5] *Amer. J. Surg.*, 1947, **73**, 37.
[6] *Canad. med. Ass. J.*, 1952, **67**, 58.
[7] Montgomery, R. M., and Nachtigall, H. B., *Postgrad. Med.*, 1950, **8**, 401.
[8] Westcott, F. H., *N.Y. St. J. Med.*, 1950, **50**, 698.
[9] Mitchell, W., *Retail Chemist*, 1952, **23**, 27, 65.
[10] *J. Lab. clin. Med.*, 1938, **24**, 230.
[11] *Medical Physics, Chicago*, 1944, p. 172.
[12] *C.R. Soc. Biol. Paris*, 1928, **99**, 1683.
[13] *Ned. T. Geneesk.*, 1951, **95**, 208.

drying of the secretion, and he thought it more probably due to stimulation of the cilia. Thus it is possible to observe how easily the theory of the action slips from what is rational and has some foundation to simple speculation.

Certainly neither the bacteriostatic action nor the stimulation of cilia can explain the efficacy of oral chlorophyll preparations in reducing perspiration and other body odours, which is widely claimed. Thus le Vann[6] has stated that in a mental institution the commonest reason for resignation of staff was the smell from incontinent patients. The patients were separated into two wards and given tablets of a chlorophyll derivative, all antiseptics being removed. There was a striking reduction in the smell. Must we then suppose that chlorophyll prevents incontinence? Reports of this kind, and those relating to reduction of underarm odour in industrial workers and college athletes,[7 8] are very difficult to understand and to credit. This is particularly so when these authors make tests to show that "raw chlorophyll" and a "copper salt of chlorophyll" are insignificantly active compared with the "specially prepared chlorophylls."[7]

The composition of these chlorophyll extracts is not known. Apart from the fact that in the tests reported no descriptions of the preparations have been given, it is very difficult to analyse extracts of this kind. The water-soluble chlorophylls which have been marketed for many years as colouring agents contain the alkali metal salts of the acids (chlorophyllins) which result from alkaline hydrolysis of chlorophyll (chlorophyll is esterified by a methyl and a phytyl group). Only the salts are soluble in water. The free acid and the ester are very insoluble. In the known extraction processes much of the magnesium of the original chlorophyll is likely to have been removed, and copper may have been substituted. Methods of standardization have been developed for measuring the colour only, but simple methods for analysis of the constituents are not available.[9]

If, as seems likely, the proprietary preparations recommended to combat odour contain chlorophyllin salts they would be precipitated in the stomach as the insoluble free acids. The extent of absorption and the metabolic fate of chlorophyll and its derivatives in man have not been fully elucidated. Certainly a large part is excreted as phaeophytin in the faeces. Brugsch and Sheard[10] recovered 77% in this form in one case and 43% in another when 400 mg. of crystalline chlorophyll-a was given. The remainder could not be accounted for. Degradation products related to phylloerythrin were found in the bile, but it was not certain that they arose from the ingested chlorophyll. Urinary coproporphyrin was increased only from 80.6 μg. to 113.6 μg. by chlorophyll feeding, whereas that in the faeces increased from 48.6 μg. to 770 μg.

The action of chlorophyll in the tissues can only be surmised. Glasser[11] quotes a report[12] that chlorophyll increases respiratory metabolism in a way similar to thyroxine. Westcott[8] showed that the water-soluble extracts removed the smells of certain chemicals—benzyl mercaptan, sodium thioglycollate, and trimethylamine—when incubated for five minutes at body temperature. Djikstra[13] found that the smells of rotting cheese and vitamin preparations were removed by incubating with soluble chlorophylls for 24 hours at 50° C. Chlorophyll derivatives might therefore modify metabolism or react with specific compounds, such as strong-smelling sulphur compounds, with a resulting decrease in odour. But this can be no more than a guess about the mode of action of a substance which is unidentified, is difficult to characterize and to trace in the body, and is claimed to produce an effect which cannot be assessed in any way but by subjective impression.

BASIS OF CHROMATOGRAPHY

One of the earliest achievements of chromatography was to show that the russet tints of autumn leaves are present even in spring, beneath the green mask of chlorophyll. All the colour of a young leaf will dissolve in an organic solvent such as petrol. To continue this experiment one then took a long glass tube and packed it nearly full with a dry powder such as aluminium oxide, set the tube vertically in a clamp, and poured the solution of leaf pigments into the top. Slowly and evenly the solution percolated into the powder, and as the last drop sank into the column clean petrol was poured on top and also began to percolate down. Eventually it began to drip out of the bottom of the tube below the packed oxide. If one then looked to see what had become of the leaf colour, one saw a series of coloured bands at different points along the column, all slowly moving to the bottom, but at different rates. Nearest the top and slowest were two green bands, the chlorophylls; in the middle came the reddish-brown xanthophyll, while fastest of all and nearest the bottom was the yellow carotene. Ultimately the different substances thus revealed in the green leaf emerged separately in solution from the bottom of the column. Chromatography is thus a technique by which coloured substances can be made to declare their individual presences in a mixture, and by which they can be separated and purified. Since this experiment of nearly 50 years ago other solvents have been tried and other powders used to make the column. But very few powders have been

[1] Balston, J. N., and Talbot, B. E., *Guide to Filterpaper and Cellulose Powder Chromatography*, 1952, London.
[2] Gross, J., and Pitt-Rivers, R., *Lancet*, 1952, 1, 439.

found to attract coloured substances as they move down the column, and still fewer are sufficiently selective in their attractions to make separations practicable. So adsorption chromatography—separation by differential attraction to the surface of a powdered solid—has not had a very wide use.

Just about 12 years ago Drs. R. L. M. Synge and A. J. P. Martin (see annotation on next page) invented a new form of chromatography. Instead of attraction to a solid surface they used attraction into water as a separation process. But water will not form a column like a dry powder: it is too cohesive to let another solvent penetrate it, and too restlessly fluid to avoid at once mixing together any separated substances. So to make a "water column" it was necessary to provide an inert scaffolding, to use damp shredded paper, or, better, silica gel, where the silica acted merely as a skeleton to hold the water still, erect, and penetrable. If mixed colours in an organic solvent were poured on the top of this column again a series of separated, slowly moving coloured bands appeared, but this time it was solubility in water which held the colours back. The more soluble they were, the more they were attracted out of the moving organic solvent into the stationary water. The extent to which a substance distributes itself between each of any pair of solvents is called its partition coefficient, and since even similar substances nearly always have different partition coefficients a separation is nearly always possible by this partition chromatography. The new method therefore has a much wider application than the old.

Even colourless substances can be made to show on the column provided they are acid or alkaline. It is only necessary to add a little indicator beforehand to the silica gel—for instance, a little bromcresol green, which gives it a bluish colour. Suppose now a solution of mixed fatty acids (acetic, propionic, butyric, and so on) in chloroform is put on the silica gel column. As it penetrates downwards the acids are extracted to difference degrees into the stationary water layer, and being acids they mark their presence by turning the indicator yellow. Thus in a little while a series of yellow bands appears on the blue column, slowly moving down to the exit. They move because the organic solvent is moving and because each acid never stays finally in the water but all the time apportions its existence between the two solvents. When a little almost pure chloroform goes by some of the acid moves back into it, and all along the column, as the conditions alter, such exchanges are going on, back and forth, so that whatever quantity of acid is present it is always strictly apportioned between the two solvents in accordance with its partition coefficient.

This new chromatography has already proved immensely valuable in the isolation of vitamin B_{12} and of antibiotics and is providing the key with which to lay bare the detailed structure of such proteins as A.C.T.H. and insulin. In a simple modification, paper chromatography, it is becoming of use to the clinical pathologist and clinician. In this a strip of blotting-paper or filter-paper replaces the silica jelly in its glass tube. A tiny drop of the solution to be studied, perhaps an extract of urine or plasma, which has been freed of interfering organic salts, is placed at a marked place at one end of the paper strip and allowed to dry. Then that end of the paper is dipped into a trough of organic solvent such as butyl alcohol or collidine and the whole system enclosed in a box or jar to prevent evaporation and disturbance. Slowly the organic liquid creeps along the paper, and as it passes the dried spot it draws the mixed substances with it; they travel at different rates according to their partition coefficients, for there is enough moisture in the paper to provide a water phase alongside the organic solvent. After several hours the substances are spaced at different points along the paper, and if they are colourless they can sometimes be revealed by ultra-violet light or radioactivity, or by chemical test. The distance each one has moved, compared to the distance travelled by the solvent front in the same time, is a ratio called the R_f number, which is characteristic for the substance in that solvent. Thus an unknown substance may be identified by comparing its R_f numbers in several solvents with those of pure substances. This avoids the need also to present photographs of each experiment carried out.

Paper chromatography has already been used to study sugars, vitamins, fatty acids, nucleic acids, and other substances of medical interest in plasma, urine, plant juices, and tissue extracts.[1] In conjunction with radioactive iodine it has made possible an examination of all the iodine-containing compounds present in normal plasma, from which it appears very likely that the true thyroid hormone is not thyroxine but 3.5.3′-L-tri-iodothyronine.[2] It is a cheap, simple method which is very little bother and suitable for very small quantities. It can be only a matter of time before it is standard equipment in every large hospital laboratory.

WINTER SLEEP

Where do flies go in the winter-time? The answer is rather an anticlimax after the song. Those that do not die creep into cracks and crevices and sleep the winter out. So do the butterflies that make their appearance in the early spring. The snail seals up the door of its shell; the earthworm burrows deeper into the warm earth. Some fishes bury themselves in the bottom mud when their water freezes; others remain active until the water solidifies around them and survive the trap, provided they are not held too long and the temperature does not fall further. The danger to most living creatures is that the water of their tissues will crystallize as ice and destroy the structure of their cells. But its freezing-point may be lowered below that of fresh water by the presence of salts and other dissolved substances: proteins in particular have a restraining effect on ice formation and encourage supercooling. And so it is that even the Antarctic has life[1]—mosses and lichens, mites, insects, and crustaceans—wherever the water melts for a short time.

It is the warm-blooded creatures like man which cannot stand the cold. Rabbits, cats, dogs, guinea-pigs, monkeys, and rats have been cooled to (rectal) tempera-

tures of anything from 19° C. (66° F.) to 10° C. (50° F.) and have died.[2] Patients with painful malignant disease have been cooled to about 28° C. (82° F.)—crymotherapy—at which temperature they are unconscious and the pulse and blood pressure imperceptible, so that it seems likely that much lower would kill them. At least one factor in the death of cats and rats is that their nerves cease altogether to conduct impulses at a temperature of 9° C. (48° F.). The animal therefore becomes disorganized when its body cools to this temperature.[2] The higher mammal is an animal needing a certain constancy of internal environment. It functions only with a steady body temperature, a steady blood glucose level, a steady osmotic pressure and ionic composition; perhaps higher cerebral function is possible only with these constant conditions, for life does not demand them. Primitive mammals, such as echidna, the spiny ant-eater from Australia, have only a rudimentary temperature control,[3] and tend to cool off when the weather gets cold. Bats, strangely enough, have no control at all,[4] and are really cold-blooded mammals. But in order to fly in cool weather they have to work up a body temperature by some minutes of shivering, and in real cold they sleep.

Going to sleep for the winter is a way of economizing on food. True hibernation is confined to certain rodents and insectivores, such as the dormouse, hedgehog, ground squirrel, marmot, and golden hamster. During the spring and summer they are normal warm-blooded mammals, but in the autumn their temperature control begins to break down and they sleep, at first for odd days, then more regularly, finally all the time. Body temperature now drops as environmental temperature drops, and the physiological responses are all changed. The respiratory centre becomes insensitive to carbon dioxide, which accumulates in the blood, for the animal may take only one breath in three minutes. The blood-sugar level drops, and the animal slowly metabolizes its body fat, in particular a special adipose tissue between the shoulder-blades. The heart beats very slowly; in the hamster with a normal beat of about 500 per minute the rate may fall to as low as 8.[5] In the hamster, and probably in other hibernators, the nerves continue to conduct down to 2° C. (35.6° F.).

But this sleep is not absolute. Marmot and ground squirrel waken occasionally to defaecate, and sometimes to look for food. All will waken if they are in danger of freezing, while electric shocks, sudden heat, and even noise will also startle them into heat production. This is usually very rapid; the dormouse's body temperature has been known to rise 19° C. (34° F.) in just over 40 minutes. Part of the natural waking stimulus in spring seems to be finding food again. A dormouse normally sleeps about six months, but in a cold laboratory and without food it has continued over a year.

But environment is not the only factor in hibernation. The thyroid, the pituitary, and in particular the adrenal cortex show a cycle of histological changes throughout the year. Hypophysectomy has resulted in hibernation, though followed in a few days by death,[3] and it is possible that the hypothalamus also was damaged. It is thought that the temperature-regulating centres of the hypothalamus control hibernation[5] through the pituitary and adrenal cortex, damage to which leads to hypothermia in man. But much research remains to be done on hibernators, and its results may well clarify our understanding of temperature control in patients.

1 Bertram, G. C. L., *Arctic and Antarctic*, 1939.
2 Chatfield, P. O., *et al.*, *Amer. J. Physiol.*, 1948, **155**, 179.
3 Kayser, C., *Biol. Rev.*, 1950, **25**, 255.
4 Hock, R. J., *Fed. Proc.*, 1951, **10**, 65.
5 Chatfield, P. O., and Lyman, C. P., *Amer. J. Physiol.*, 1950, **163**, 566.

NOBEL PRIZE FOR CHEMISTRY

The announcement last week by the Swedish Academy of Science that two British biochemists Dr. A. J. P. Martin and Dr. R. L. M. Synge are to share this year's Nobel prize for chemistry is an occasion for congratulation. The award, valued at £11,400, is for their work on partition chromatography, which was done in collaboration at the laboratories of the Wool Industries Research Association in Leeds. Martin and Synge now work separately, the former at the National Institute for Medical Research, Mill Hill, and the latter at the Rowett Research Institute, Aberdeen.

The importance of their invention was quickly recognized, and both were elected Fellows of the Royal Society in 1950. Their achievement consists essentially in the inspired application of a few simple physical principles to problems of separation. Even at its present stage of development chromatography has provided one of the most powerful analytical tools at the disposal of chemical science; by no methods other than those coming under its general heading can closely similar substances be separated from one another with such efficiency (see annotation on page 1087). In the hands of Martin and Synge themselves and in those of other workers the methods evolved have so far found their most effective application in biochemistry; it was indeed interest in the long-standing problem of separation of amino-acids that provided the initial stimulus for the work, and it is in this particular field that chromatography has achieved some of its greatest triumphs. The ramifications of all that is now understood by chromatography penetrate, however, into every corner of chemistry and even into atomic research. Since the effective chemical and biological study of natural products can be undertaken only after their complete purification, the importance of chromatography for the advance of chemical, biological, and medical research is self-evident. Many problems have already been solved by its aid; many more even more subtle will undoubtedly be solved, though an approach to their solution could not even have been contemplated had it not been for the work of the Nobel Laureates in Chemistry for 1952.

We announce with regret the death on November 8 of Air Vice-Marshal Sir David Munro, Director of R.A.F. Medical Services from 1921 to 1930, and Secretary of the Industrial Health Research Board from 1930 to 1942.

REFRESHER COURSE FOR GENERAL PRACTITIONERS

THE DIAGNOSIS OF SMALLPOX.—II

BY

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Variations in the Rash

Two factors influence the character of the rash in smallpox—the resistance of the individual and the virulence of the virus.

Resistance of the Individual.—Here, previous vaccination is the most important factor. With the passage of time immunity wanes, and should the disease be contracted its whole course may be "modified." It is not untrue to say that to those unacquainted with the disease this term implies a simple alteration in the number of lesions—the more modified, the sparser the rash. Such a concept is only a part truth and from a diagnostic point of view may be dangerous. Previous vaccination can alter not only the number but the whole character of the lesions; only one factor may remain constant—the capacity to infect susceptible persons with the most severe form of the infection. In particular, stress might be placed on the following points:

(1) Although generally the number of lesions is greatly reduced, an almost confluent form may be encountered in previously vaccinated persons. The element of the eruption, however, is much smaller, and, despite the profuseness of the eruption, the secondary toxaemia is never profound and scarring is greatly reduced. Many of the lesions fail to become vesicular.

(2) In the more resistant subject, the individual lesions are less deeply situated in the skin. As a result the progress from stage to stage is more rapid. In such a case the metamorphosis from papule to pustule may take place in twenty-four to forty-eight hours.

(3) Some of these softer, more superficial lesions may progress from papule to scab so rapidly that lesions are present at different stages and a superficial appearance of cropping is presented. Such an appearance is enhanced by the abortion of some of the lesions at the papular stage. It is possible, in fact, that a certain amount of cropping may occur in such cases, successive papules occurring over a period of three to four days, so increasing the resemblance to chicken-pox. (In this connexion it is worth while pointing out that on rare occasions the chicken-pox virus may be attracted to traumatized skin. This has been seen, for example, in a theatre nurse whose arms and hands were affected by scrubbing and disinfectant irritation; or in a child around the buttocks or lower abdomen where the skin was excoriated by neglect.)

Virulence of the Virus.—The virus of variola major has preserved throughout its history an almost uniform virulence, so that variations in the severity of the disease which it produces are almost entirely explained by variations in the resistance of the host. The virus of variola minor, on the other hand, is one which has been shorn of much of its attacking power. As a result, it produces a mild form of smallpox (alastrim) irrespective of the state of resistance of the host; and, moreover, this mildness "breeds true," so that susceptible contacts are also affected by a more or less non-fatal illness. But it is still smallpox: and a modified attack of variola major due to enhanced host-resistance may be indistinguishable from an attack of variola minor due to a virus of reduced virulence. This point is worth emphasizing, for it means that the important features of the disease which have been described above are true for both forms.

As with the modified disease, we may expect to observe in alastrim differences in the individual elements and their evolution. In the first place they are usually smaller and more superficial, so that their shape is much less uniform. Their evolution is much more rapid and the pustular stage may be reached on the third or fourth day. The vesicular stage is of very short duration, and indeed may escape detection. But, no matter what alterations there may be in the character of the eruption, the rash still shows the pattern of smallpox. It is a symmetrical rash, affecting the face and limbs more than the trunk, the extensor aspects rather than the flexor, the prominences rather than the sheltered areas.

Vaccination

Recent successful vaccination is an absolute protection against smallpox. This might well be treated as a text for an old-fashioned sermon which would then develop the theme under three heads—recent, successful, and vaccination.

Duration of Vaccinial Immunity.—No form of artificially acquired immunity is lifelong. It should therefore occasion no surprise that, with the passage of time, the immunity conferred by vaccination wanes. It seems probable that the duration of immunity is related to the extent of the primary stimulus, and that this in turn may be related to the amount of skin involved in the vaccinal reaction. In recent years the tendency has certainly been towards a reduction in the amount of skin trauma involved in the operation. It may be that this minimal form of vaccination reduces the duration of complete protection. Whether this is true or not, it is certainly the case that there is great individual variation in the length of the immune period. As a broad generalization, it may be accepted that successful vaccination gives a guarantee of immunity for one year and probably for three years. Some degree of resistance may remain for from 10 to 20 years or even longer. Workers who may be exposed to the disease should be vaccinated annually. But "recent" must also include reference to exposure. Ricketts taught that successful vaccination within the first seven days of exposure would often prevent an attack, and many people remember this dictum loosely and believe that it states an absolute truth. But Ricketts, right in this as in so many other areas of our knowledge of smallpox, stated that what really mattered was not when the patient was vaccinated but when the vaccination "took." For complete protection successful vaccination must be attained before exposure takes place. While immediate vaccination of contacts must constitute an important aspect of smallpox control, too high a measure of protection must not be expected.

Successful Vaccination.—When an individual is vaccinated for the first time the success of the measure is easily established. After a degree of local irritation and itching the inflammatory reaction in the skin increases and between the fifth and seventh days a typical vesicle appears, which then proceeds to pustulation and scabbing. The reaction is accompanied by inflammation of the area, enlargement of the associated lymph nodes, as well as some degree of constitutional disturbance which is usually greater in the adult. When revaccination is carried out the degree of reaction will depend upon the amount of immunity remaining from the previous operation. After a long period of years there may be nothing to distinguish the result from a primary response; performed on a person more recently

vaccinated, the lesion may pass through its stages more rapidly, so that vesication appears on the third or fourth day (accelerated reaction). In some persons there may be no reaction.

In such a situation it is of course dangerously simple to regard an absence of response as indicating remaining immunity from previous vaccination. But a moment's consideration shows that this is indeed fallacious. In the first place, the lymph may have been carelessly stored or may have been faulty in some other way and incapable of producing a successful "take." In the second place (perhaps the commonest reason), the operation may have been imperfectly conducted. And finally—although this point is not fully proved—one gets the impression that an area of skin may, from frequent revaccination, become unreactive. If the person who is revaccinated is likely to come in contact with smallpox, absence of "take" must be regarded with suspicion. The operation should be repeated, with fresh lymph, on a new site and the reaction observed every 24 hours. Itching or irritation is usual, and a papule, often with minute vesication, forms within 24 to 48 hours. The unfortunate term "reaction of immunity" should not be used, because of the difficulty which arises in its interpretation. In some cases there is no doubt that it can be simulated by a reaction due to sensitization to the calf lymph.

Vaccination Technique.—The multiple pressure method of vaccination should be adopted. It is simplest to perform, is almost painless, causes least trauma to the skin, and is relatively free from severe local reaction. The skin site should be prepared by cleansing with acetone or ether, and care should be taken to see that the skin is dry before applying the drop of lymph. A number of pressures are made rapidly with a sharp Hagedorn or cutting needle held parallel to the skin surface. For primary vaccination 15 to 20 pressures are adequate; for revaccination 25 to 30 pressures should be made. The excess lymph can be wiped off with a piece of clean wool. No dressing is required. In the case of primary vaccinations the site should be inspected after one week; in revaccinations the patient should be asked to report on the second or third day. Comment may be made on one point of technique. There seems no doubt that some people still eject the lymph from the capillary tube by blowing through it with the mouth. This is a most reprehensible practice. A rubber teat should always be used. So far as is humanly possible vaccination should be conducted as an aseptic operation.

Laboratory Diagnosis

Although, almost as a *tour de force*, the virologist may demonstrate the presence of virus in the blood or throat during the prodromal toxic illness, from a practical point of view it is at the stage of eruption that his help will usually be sought. His tests will concentrate on two points: isolation of the virus, or demonstration of its presence by a serological test. One or other of the tests can be applied at any stage of the rash.

Microscopical Examination for Elementary Bodies.—Absolutely clean dry glass slides are required. With the blade of a scalpel the lesion is scraped sufficiently to produce a little "juice"—not blood. This is transferred to the glass slide and a thin smear made with it. Material from several lesions is taken and a number of similar smears are made. Six may conveniently be arranged along the length of the ordinary microscopical slide. If possible, several slides should be sent; up to a point, the more material supplied, the more chance is there of an accurate result. *The slides must not be heated.* After suitable staining the smears are examined under the oil-immersion lens of a microscope. In a well-taken preparation the elementary bodies are easily seen in considerable numbers. There is no doubt that the success of this examination is directly dependent on the care with which the slides are prepared. Attention to detail is therefore essential: the slides must be rendered completely clean, vigorous scraping of the lesions must be avoided, blood must not be drawn, and purulent lesions must be avoided. This method is therefore best suited to the early stages of the eruption; once pustulation has formed, the presence of cell debris, micro-organisms, and pus cells may make interpretation very difficult. Further, while a positive result—which will be available within a few hours of the receipt of the specimen—is of great value, a negative result cannot be regarded as excluding the diagnosis of smallpox.

Isolation of the Virus.—This can be attempted at any stage of the eruption. Material may be submitted on glass slides, as already described, in capillary pipettes from vesicular or pustular lesions, or in screw-capped containers in the form of scabs. The chorio-allantoic membrane of the developing hen's egg is inoculated with the specimen after appropriate treatment. Two to three days later examination of the membrane visually will often be sufficient to make a diagnosis, although in doubtful cases further procedures may be necessary. This method is precise and highly accurate. Its only disadvantage is the time which it takes.

Complement-fixation Tests.—The presence of virus antigen may be shown in vesicular or pustular fluids or crusts by complement fixation. For this test fluid from vesicles is preferable, but thick smears on glass slides will also suffice. This is a rapid test which can be conducted in less than 24 hours, and has a high degree of accuracy.

These tests have added greatly to the precision of smallpox diagnosis. Like all biological tests they have their limitations, and no virologist would rely absolutely on any single test. With a reasonable amount of well-taken material all three may be performed as a routine. The actual demonstration of the virus growing in the chorio-allantoic membrane naturally gives the most conclusive proof of the diagnosis and is really essential for the differentiation of variola and vaccinia.

Summing-up

The diagnosis of the florid case of smallpox is comparatively easy. If the individual has some residual immunity from previous vaccination (modified smallpox) or is infected by a virus of reduced virulence (variola minor) the character of the eruption may be so altered as to make a correct diagnosis very difficult. In such cases the greatest reliance must be placed on the distribution of the rash—general and focal. The pattern of the rash is constant; when in doubt make an actual diagram and count the lesions in the different regions. Too much attention must not be paid to the traditional diagnostic points such as shottiness, size, shape, presence of umbilication, appearance of cropping, and lesions in the mouth or on the palms or soles. The doubtful case will be the modified case, and any or all of these points may prove unreliable. For this reason no mention has been made of the presence of vaccination scars; in the cases in which doubt arises scars are usually present and their presence may prove illusory.

The question to be answered by the clinician when confronted by a doubtful case, as Wanklyn has pointed out, is, Can this be smallpox? If the answer, reached after consideration of all the evidence gleaned from a careful examination of the whole patient, is "Yes," then the case must be regarded as one of smallpox and all necessary steps taken as required by the local medical officer of health. For, despite the emphasis placed upon the valuable aid which can be given by the laboratory, the final decision must be a clinical one. The analogy of diphtheria—preached by every fevers clinician for the past half-century—is apposite: when in doubt you submit a swab, give serum. So to-day in smallpox the decision to set in motion the administrative machinery of the public health service must rest with the clinician. When in doubt you submit specimens for virus examination, administer the case as one of smallpox, and inform the medical officer of health; that is the golden rule. The subsequent confirmation or

refutation of the diagnosis must nowadays lie with the laboratory. But this does not absolve the clinician from his primary responsibility. To miss the first case of smallpox in an outbreak may be a costly business—not alone in lives.

Next Refresher Course Article.—"Abdominal Hernia in Childhood," by Mr. Denis Browne.

Refresher Course Book.—The first 55 articles of this series (fully revised) are available as a book, price 25s. including postage, from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1.

A MODEL REHABILITATION AND TRAINING CENTRE

BY

HAROLD BALME, O.B.E., M.D., F.R.C.S.

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On May 24, 1952, the President of the Austrian Republic, in the presence of a large number of Government officials and other leaders, performed the opening ceremony of what is probably the finest rehabilitation and training centre to be found anywhere in Europe. It is situated at Tobelbad, in delightful wooded country about nine miles from Graz, and has been built on the site of a former spa. The original property included a famous hunting lodge and hot springs, both owned by the Government, the former containing a very fine ceiling painting—the work of an Austrian painter of the early nineteenth century—which has to be preserved as a national trust.

Extensive new buildings have been erected over the site of the hot springs, affording ample accommodation for 250 patients as well as the staff of the centre. The river has been deflected from its former course and banked with stone, so as to pass through the grounds and provide a constant water supply.

These buildings have been put up and are owned by the Allgemeinen Unfallversicherungsanstalt (the United Accident Insurance Corporation), and it is an interesting fact that their decision to establish this splendid centre, and to offer first-class opportunity for the rehabilitation of accident cases occurring anywhere in Austria, was largely influenced by the arguments submitted to them by two young orthopaedic surgeons who were members of the first Rehabilitation Course held in this country under the auspices of the British Council. These Austrian surgeons were so impressed by the economic value of modern methods of rehabilitation and vocational training that on their return to their own country they succeeded in persuading the United Accident Insurance Corporation to buy the Tobelbad property and erect a rehabilitation centre on the British model. Since that time the medical director of the centre, Dr. Georg Neubauer, has also attended a course on rehabilitation in Great Britain during a period of two months, and it is a great compliment to this country that the organizing, staffing, and equipping of this splendid centre have closely followed the British pattern.

Rehabilitation Centre

This is a large modern four-story building, with an attractive curved front and wide balconies, each provided with fitted window-boxes filled with geraniums, petunias, and other flowering plants. The wards are small—usually for three or four patients—and are light and attractive, with good beds, lockers, and other amenities, and each opening out on to the balcony.

In addition to a large dining-room for ambulatory patients, modern kitchens, and excellent administrative and medical offices, the centre contains the following special departments:

(*a*) Plaster- and dressing-rooms, for applying or changing plasters and dressings.

(*b*) A small operating-theatre. (All cases requiring major operation are transferred to Graz Accident Hospital.)

(*c*) A well-equipped *x*-ray department.

(*d*) A clinical laboratory.

(*e*) Physical medicine department, with large and excellently equipped rooms for massage, electrotherapy, actinotherapy, electromyography, and light treatment.

(*f*) Two remedial gymnasia, the smaller one being furnished with wall bars, rings, and other apparatus for individual treatment and exercise; the larger one being equipped for group exercises. Both have wooden floors, special mats for floor exercises, walking-handrails, mirrors, suspension beam, and wall bars.

(*g*) Extensive and excellently equipped hydrotherapy department, including: (i) A large warm swimming-pool, fitted up for exercises and games; (ii) a small warmed bath, on the principle of the Hubbard tank, for individual exercises; (iii) a series of four long ankle-deep "walking-baths," one containing hot water, one cold water, one soft mud, and the other moist sand; (iv) individual baths and showers.

(*h*) A small occupational therapy department.

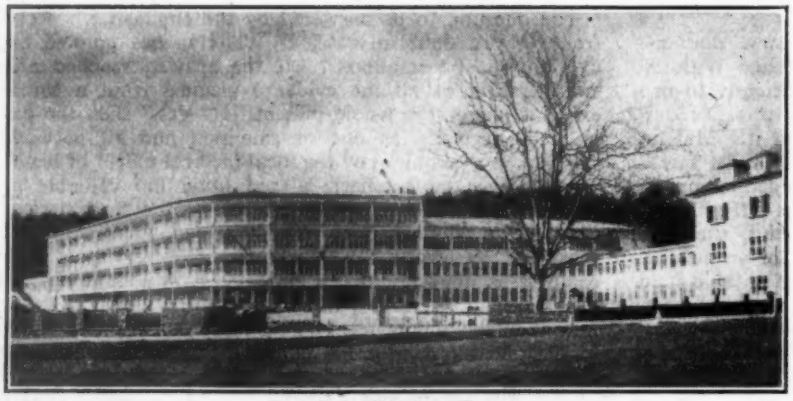
(*i*) An indoor play-room, with table tennis and other games.

(*j*) Outdoor sports grounds, with facilities and apparatus for archery, football, volley-ball, basket-ball, outdoor gymnastic exercises, and with paths provided with obstacles, both on the flat and through a wooded hill, to train patients in walking over rough and uneven ground after injuries to ankles and feet.

(*k*) A small prosthetic workshop, for the manufacture of temporary and permanent prostheses and other mechanical aids.

Vocational Training Centre and Accessory Buildings

This separate building is connected with the rehabilitation centre by wide covered-in passages, well decorated and with parquet floors, and containing a series of light, well-equipped class-rooms and workshops. These rooms, when completed, will be used for short courses of training in carpentry, metal work, wood-carving, leather work, shoemaking, tailoring, dressmaking, etc. It is not intended to use them for long or complete vocational training courses, such as are available in Government training centres, but rather as a means of giving both work therapy and vocational guidance to those undergoing physical and industrial rehabilitation before returning to their former employment or undertaking new courses of training. This vocational training centre may thus be regarded as an attempt to combine the main features of the Luton rehabilitation departments and an industrial rehabilitation unit.



The Rehabilitation Centre

The accessory buildings include a church, nurses' home, staff quarters, administrative block, and concert and entertainment hall.

An Excellent System

A few words must be added, in conclusion, about the system of dealing with accidents which obtains throughout the province of Styria, in which Tobelbad is situated. At the capital, Graz, a splendid modern hospital has been erected by the same United Accident Insurance Corporation, and at this hospital expert teams of surgeons, nurses, and radiologists are on duty day and night. With the co-operation of the police, the local authorities, and the Red Cross, a network of telephone call-stations has been established throughout the province, usually at the houses of Red Cross members, which are continuously manned on a rota system. At the same time a limited number of ambulance stations have also been established, prepared for emergency calls. Wherever an accident occurs in the province, no matter at how remote a spot, the local policeman is summoned and immediately rings up the nearest telephone call-station on duty for that particular day, from which messages are at once sent to the nearest ambulance station and to the Graz Accident Hospital. As a result cases are received at the hospital, on an average, in not more than two hours from the time of the incident. Expert services are there provided, including anti-shock measures, radiology, operative and post-operative treatment, and appropriate methods of medical rehabilitation. As soon as the acute stage has passed and further surgical treatment is no longer required the patient is sent on to Tobelbad to complete his course of rehabilitation away from a hospital atmosphere.

The latest news from the centre is that the accommodation is nearly all taken up; that a special department for cases of traumatic spinal paraplegia has been established on Stoke Mandeville lines; and that, in addition to cases of actual trauma, some cases of poliomyelitis and other crippling disorders are being received for rehabilitation.

MEDICAL WOMEN'S FEDERATION CONGRESS

[BY A SPECIAL CORRESPONDENT]

The Medical Women's Federation of Great Britain and Northern Ireland held its thirty-fifth Anniversary Congress on October 31 and November 1 and 2, under the chairmanship of the president, Dr. Doris M. Odlum.

The Congress began with a cocktail party on the evening of October 31 at the Royal Free Hospital School of Medicine, at which some 250 people were present. Scientific sessions were held in the morning and afternoon of Saturday, November 1, in the Great Hall of B.M.A. House.

Domiciliary Midwifery

The session was opened by the Duchess of Northumberland, who gave a short address. Then followed the Christine Murrell Memorial Lecture by Dame Hilda Lloyd. In a brilliant and provocative address the lecturer covered many aspects of her subject—"Domiciliary Midwifery." She believed that in 10 years' time there would be far less domiciliary midwifery than now, at least in the urban areas. Already a great many women preferred to have their confinements in hospitals, and she thought that this tendency was likely to increase. She discussed the advantages and disadvantages to the expectant mother and to the family group of a confinement at home or in hospital. She envisaged special hospital units which would be staffed by midwives working in conjunction with general practitioners, with specialists available in case of need. She thought that those doctors who undertook obstetric work should have some extra training and experience if they were to give their patients the best possible service.

After the lecture Dame Hilda Lloyd kindly consented to answer questions, which she did for over an hour, as her audience showed a most lively interest in her proposals. A vote of thanks, proposed from the chair, was carried by acclamation.

Child Care in the N.H.S.

At the afternoon session the care of the child in the National Health Service was discussed from various viewpoints. The opening speaker was Dr. Ursula Shelley, physician, Children's Department, Royal Free Hospital, followed by Dr. Charlotte Naish, general practitioner, York; Dr. Elspeth Warwick, senior assistant medical officer for maternity and child welfare, City of Nottingham; Dr. Sylvia K. Guthrie, consultant paediatrician, Duchess of York Hospital for Babies, Manchester; Dr. Margaret Reed, general practitioner, Cambridge; Dr. Catherine Crane, medical officer of health, City of York; and Dr. Margaret Methven, psychiatrist, Royal Edinburgh Hospital for Sick Children. Dr. Georgie Brodie (until recently deputy senior medical officer, Maternity and Child Welfare, Ministry of Health) summed up the opening papers, and the meeting was then thrown open to public discussion.

The general conclusions reached were:

(1) There was a great need for the integration of many aspects of medicine and smooth collaboration of individuals and institutions in order to provide a comprehensive health service for the child. The National Health Service Act had provided an increased opportunity for improvement and co-ordination.

(2) The improvement in the medical care of the child in Britain in the last fifty years was undoubtedly a great achievement. This country was second to none in this respect, but we should not be satisfied to rest on our laurels, as much still remained to be done.

(3) It was essential that the four services dealing with the child should act as a team, with their functions clearly defined. These were the general practitioner, the local health authority, including the school medical service, the hospital and specialist service, and the Ministries concerned.

(4) The general practitioner, who should, in fact, be the family doctor, was the backbone of the service. He could best know the environment of the child and follow its development. He would also know the family relationships and their effect on the child, and be able to assess the interplay of psychological and organic factors in illness. General practitioners needed much better training, both pre-graduate and postgraduate, in the preventive as well as the curative aspects of medicine. General practitioners were at present handicapped by lack of facilities for diagnosis such as health centres could provide with their *x*-ray, pathological, and other departments.

(5) The local health authority services had done good work in the preventive field. A valuable educational system for the mothers had been built up, and also of supervision of the young child.

(6) Health visitors could be called upon much more than they are by the general practitioner. They could give much valuable help to the family doctor, and act as a liaison with local authority clinics and the hospital.

(7) Interchange of information should be much increased by means of duplicate letters to the practitioner from the medical officers of child welfare and school clinics and by using health visitors.

(8) Most valuable pioneer work had been done in some areas by women general practitioners, who had started infant welfare clinics as part of their general practices, notably by Dr. Naish in York, Dr. Reed in Cambridge, and Dr. Hellier in Paddington (London).

(9) If the general practitioner had better opportunities for investigating the child, only cases that really needed to be seen by a consultant would be referred to hospital, whose true functions were to diagnose, to advise treatment, to promote research, and to give specialized training to paediatricians. Interchange of information was vital in this field.

(10) The Ministries played a valuable part in initiating services on a national scale, and in assuming public responsibility for them. They were essential as a co-ordinating body, but there was a tendency to over-centralization.

(11) The chief value of the National Health Service was that it had provided the child with four important facilities—the free services of a family doctor and of a consultant paediatrician in the home, free ambulance, and free hospital treatment in addition to those services previously available. There were still gaps, such as insufficient long-stay accommodation and convalescent homes. The worst fault was the inadequate co-ordination between the different services, inadequate record-keeping, insufficient exchange

of information, and the lack of facilities for investigation available to the general practitioner.

(12) It was felt that a senior woman administrative medical officer should be appointed by each large local health authority whose function it should be to co-ordinate all the paediatric services and to ensure the maintenance of a close relation between mother and child.

(13) Education of the mothers themselves was vital if they were to play their part fully in the scheme for the child's welfare and protection, and make full use of the services at their disposal.

Between three and four hundred people attended the scientific sessions, including medical guests of both sexes. In the evening the Congress dinner was held at Grosvenor House, at which nearly 500 people were present. A report of this has already appeared in the *Journal* (November 8, p. 1054). On the last day of the Congress members attended clinical demonstrations which had kindly been arranged at the Colindale Public Health Laboratory, the Elizabeth Garrett Anderson Hospital, King's College Hospital, the Marie Curie Hospital, the Middlesex Hospital, the South London Hospital, University College Hospital Obstetric Unit, and the West London Hospital.

Nova et Vetera

FATHER OF BRITISH OBSTETRICS

William Smellie: The Master of British Midwifery. By R. W. Johnstone, C.B.E., M.A., M.D., Hon.LL.D. (Pp. 139. 20s.) Edinburgh and London: E. and S. Livingstone. 1952.

Recently an eminent surgeon expressed the view that, until the later nineteenth century, the effectiveness of medical treatment had not greatly improved since Hippocrates. He would change his opinion if he would read this account of the modest, kindly, thoughtful, sensible practitioner William Smellie (1697–1763). His name is not among the great figures of medicine and he is hardly mentioned in the shorter histories. Nevertheless, by example, precept, careful observation, and sheer good sense he saved thousands of lives and rescued innumerable women from incalculable misery. Childbirth had been studied by scientific men since Aristotle, but Smellie—himself childless—was the first to apply to it the rules of ordinary measurement and calculation. He worked out beautifully and expounded lucidly the simple mechanism of childbirth. The modern practice of midwifery dates from him, and was hardly improved for a century after him. In ancient Rome women on recovery from the puerperium gave thanks to the goddess Lucina; in modern times they might do worse than offer a prayer for the soul of William Smellie.

He was born in Lanark, had a very fair general education, and was apprenticed to a surgeon in Glasgow. He began practising as an apothecary in his native town in 1720. Though without qualification or licence, he gained rapid acceptance as a medical adviser, especially for midwifery. Not till 1733 did he become a member of the Faculty of Physicians and Surgeons of Glasgow. In 1739 he decided to go to London. The fortnightly stage-coach from Edinburgh performed "the whole journey in 13 days without any stoppage, if God permits." It is possible, Dr. Johnstone thinks, that he was accompanied by his friend the novelist Tobias Smollett, and that the latter's account of the journey in *Roderick Random* is a picture of their travel. In London he rapidly obtained a practice, but his success, in accord with the whole temperament and spirit of the man, was solid and satisfactory rather than brilliant or spectacular.

Problems of Demonstrating Midwifery

Smellie was a good teacher, and his method of instruction is of interest. In the social conditions of his day, the system by which he gave professional care to poor women in their houses and supplemented it by monetary assistance in necessitous cases, in return for permission to bring pupils, was the only one possible. The problem of how to find enough suitable cases for demonstration occupied teachers of midwifery then as now. "There is," Dr. Johnstone truly says, "a sort of inverse ratio between the number of patients and the number of pupils. The greater the number of pupils the more the patients will complain and the fewer are they likely to become." Dr. Johnstone quotes the Latin poet Martial in lines which may be rendered, "I was out of sorts Dr. Symmachus and you rushed to my aid with your flock of students. I had no fever but they pawed me with their clammy hands and now I have one."

Smellie's models illustrating labour were most ingenious. The famous Dutch artist-anatomist, Pieter Camper, who attended his lectures, wrote:

"He explains the osteology of the pelvis in both a healthy and a misshapen state. He demonstrates parturition in models of which a well-grown pelvis and spine are the starting-point. Both abdominal and extra-abdominal parts have been made with such skill that not only is the structure as natural as possible but the necessary functions of parturition are performed by working models." (Abbreviated.)

The very phrase "mechanism of parturition" is Smellie's own. It occurs in print for the first time as a heading in his great *Treatise on the Theory and Practice of Midwifery*, London, 1752. The completeness of Smellie's description of the mechanism of labour is remarkable. True, he does not speak of flexion or internal rotation or extension of the head as such, but the facts are there and are well set forth. His illustrations, prepared by that excellent engraver Rymdijk, are clear and precise. Smellie was himself no mean artist, and his judgment certainly guided the hand of the draughtsman. Among his contributions was the conception of hour-glass contraction of the uterus, and he was the first to use the term and to describe the condition adequately. Smellie lived long before the very conception of asepsis, and his use of the forceps would horrify a modern obstetrician. Nevertheless, he understood their application well, and the long, curved, metal pair which he ultimately used was a great improvement on the short, straight, wooden instrument with which he began.

Smellie's Cases

The *Treatise* contains clinical records of over 500 cases, arranged in 49 "collections," each designed to illustrate a separate topic. They give a clear idea of his obstetrical methods, and he tells us that "between 1722 and 1739, while I practised in the country, I took notes of all the remarkable cases that occurred in midwifery; but in London, since the year 1740 to the present time (1754), I have been more careful and minute in forming a collection, with a view to make it public. From a great number of instances I have selected only the most material, and such as were best adapted to the nature of my plan."

In perusing these cases the reader will soon discover that they are very different from the scrupulous and impersonal records set out in modern textbooks, for they have one important point in common with a good novel. As the narrative presents one difficulty after another, strung like beads on a string, Smellie's personal character as a man emerges ever more clearly, while as a writer he is preoccupied in trying to show himself as a suitable example to his students, or occasionally as a warning. He was essentially a man of good will, kindly and tolerant towards all except those who were pretentious, insincere, or false.

We can illustrate the conditions with which he had to contend with a single example. Some of the scenes which he conjured up are worthy of Hogarth in their stark realism. Consider this:

"In the beginning of my practice I was sent for in a cold frosty night to a poor woman at some distance in the country, who had been safely delivered. As she was excessively cold all the time of labour, from the badness of the house, the want of clothes and necessaries of life, I gave her husband money to go to an alehouse at a mile distance and bring something comfortable. I left directions with the midwife to get her warm as soon as possible. The fellow got drunk and did not return for several hours. I was told afterwards that the cold and shivering continued, and the poor creature died next morning. Indeed as there was little or no fuel for fire, both the midwife and I caught

severe colds; for it was a lone house and at a distance from any inhabited neighbourhood."

Again, there is a definite aroma of Gin Lane in Case 463:

"A poor woman in St. Giles's was delivered by Mrs. More and some of my pupils, who gave her some money; which being soon spent in gin with her gossips, she went out begging with her child on the fourth day after delivery, was taken with violent pains and a fever that night, and with great difficulty recovered by blooding and antiphlogistic medicines."

A very great help to practitioners in his day was his magnificent *Set of Anatomical Tables* issued in folio in 1754 as an obstetric guide. It was provided with figures by Rymdijk and Camper, the originals of which are now in the University of Glasgow. Dr. Johnstone's book provides a most readable account of the possibilities of extending scientific and clinical knowledge which are open to the right kind of practitioner without any institutional backing. It is, however, a pity that the work is not better indexed and is without a bibliography. Perhaps on this account the reviewer has been unable to find in it reference to "Erb's palsy," which Smellie is said to have been the first to describe.

CHARLES SINGER.

Preparations and Appliances

SUCKER APPLIANCE FOR CLEFT-PALATE SURGERY

Mr. W. G. Holdsworth, F.R.C.S., of the Plastic and Jaw Unit, Rooksdown House, Basingstoke, writes: With conventional suction appliances an accurate estimate of blood loss during operation is not possible because of the length of tube between the nozzle and the bottle, and for the same reason small amounts of blood cannot be measured. The latter consideration is of prime importance where the patient is an infant, and has led me to have constructed the device here illustrated.

The nozzle leads direct into a glass reservoir, capacity 200 ml., which is connected by a stout rubber tube to a suction machine. The reservoir is a graduated bottle of standard type, and therefore readily replaceable, and is of such a size that it can be conveniently held in the hand and used to direct the nozzle to the operation site. Swabbing or washing of the wound would of course invalidate the reading. The apparatus was designed for use in cleft-palate surgery, in which neither of these procedures is necessary. The appliance was constructed by Messrs. Charles King Ltd., of Devonshire Street, London, W.1.

Correspondence

Because of the present high cost of producing the Journal, and the great pressure on our space, correspondents are asked to keep their letters short.

Specialists in Physical Medicine

SIR,—Your leading article on the development of consultant services (November 1, p. 984), and in particular your reference to the need for physical medicine specialists, underlines the inadequate provision made for this specialty in the National Health Service.

Since the war there has been, and there continues to be, a large increase in the number of cases referred for physiotherapy. In one London teaching hospital alone in the last five years the number of patients referred has grown from 6,764 to 11,861 a year. This is an increase of 75.3%, and compares with an increase of 6.7% for the total hospital out-patients in the same period. Although this inundation is derived partly from the new-found popularity of physiotherapeutic treatments with patients and general practitioners alike, it is largely due to the widening scope of physical medicine. This specialty is now responsible for the diagnosis and treatment of many disorders of the locomotor system and the application of physiotherapy and rehabilitation.

To direct existing physiotherapy departments and to continue research work, the present complement of physical medicine specialists is quite inadequate. It is not generally realized that there are only about 60 doctors who possess the Diploma of Physical Medicine. That the Ministry of Health should have thought it possible to maintain the number of consultants in this field at an adequate level by two appointments a year, while limiting senior registrar posts to about 10 for the whole country (H.M. Ref. 94112/1/27), is evidence of its utter failure to appreciate what is required to meet the present situation. Until physiotherapy is fully supervised by physical medicine specialists, with adequate training, we shall continue to spend large sums of money on ineffectual physiotherapy. If more registrar posts are not created, the present number of doctors with five years' or more experience and with qualifications in physical medicine will soon be absorbed into consultant practice. Who, then, will undertake the supervision and training of physiotherapists?—I am, etc.,

HORDER,
London, W.C.2. President, British Association of Physical Medicine.

Geographical Distribution of Cancer

SIR,—I have with interest seen the paper by Mr. C. D. Legon (September 27, p. 700) on the subject of geographical variations in the mortality of cancer. It is often not realized that this discipline dates from 1846, when Walshe reported on cancer figures from London as far back as 1728, and discussed the occurrence of cancer in Algiers, Calcutta, China, Copenhagen, Egypt, Hobart, Massachusetts, New York, and Senegal.

The shortcomings in reliability of the diagnosis of cancer, however, invalidated research of this kind even up to 1939. The elimination of inaccuracy in various diagnoses has made it possible to work out reliable statistics on many types of cancer, although it seems as if gastric cancer may be among the types least accessible to accurate demographic study. In 1950 a symposium on the subject of the geographical pathology and demography of cancer met in Oxford under the auspices of the Council for International Organization of Medical Sciences, and with the president of the latter organization, Professor J. Maisin, in the chair. Britain was represented by Sir Ernest Kennaway, Dr. Richard Doll, Professor B. S. Platt, and Dr. Percy Stocks. This meeting succeeded in making a sketchy survey of variations in the frequency of cancer which may be sug-

gested in various parts of the world, and made recommendation for further study. To produce final evidence is, however, a most complicated matter, since cancer increases in frequency with age, so that it will be necessary to have detailed knowledge on the age distribution of the normal population as well as of the cancer patients before final conclusions can be drawn.

The International Cancer Research Commission has established a committee on geographical pathology which endeavours to promote endemiological studies on cancer in various parts of the world. In July this year a symposium met in Louvain for the discussion of the endemiology of cancer of the lung (*Lancet*, 1952, **2**, 581), and the committee is assisting the International Society for Geographical Pathology in the preparations for a world-wide review of cancer frequency and mortality to be made at a conference in Washington, 1954. It would seem that this field of investigation will deserve far more attention by research than has been given to it in the past by the various bodies set up for research in cancer. It has to be realized that as long as factors causing cancer are described as "geographical" this means that our knowledge of their nature is entirely unsatisfactory. Attention should certainly be paid to observations like those published by Mr. Legon, even if the explanation of the variation may have to be sought in quite unexpected fields of study.—I am, etc.,

JOHANNES CLEMMESEN,
Director of the Danish Cancer Registry.

Biochemical Normals in Healthy Africans

SIR,—Africans often consume an inadequate diet, and parasitic diseases and disorders and the infections which are linked with unfavourable environmental and social conditions are common enough. It is not surprising, therefore, that various abnormalities are encountered among these people—in the biochemistry of the blood protein picture, in liver function tests, in carbohydrate metabolism, in the excretion of ketosteroids, and so forth. The question naturally arises, What are these abnormalities due to? So many factors could be involved—for example, racial differences; acute episodes of unsatisfactory feeding (for example, at weaning time); chronic undernutrition and malnutrition; habituation to a high cereal diet very low in animal protein; chronic malaria, schistosomiasis, or ankylostomiasis; syphilis, tuberculosis, etc. All too often several of these possible influencing factors are present simultaneously—a state of affairs rendering it very difficult to investigate the role of any one of them. There is thus a serious lack of biochemical data on Africans accustomed from birth to a satisfactory diet, and who have been, and are, free from infestations and infections. It is possible, of course, to collect ample information on Africans fed a satisfactory diet for a limited number of years, and Bantu nurses, for example, are being studied at a local non-European hospital; nevertheless, uncertainty of their nutrition in infancy, childhood, and youth, and of the incidence of parasitic and other diseases occurring during this period, precludes them from supplying the fundamental data so urgently required.

With this problem in mind, we have recently visited a small, very isolated group of villages at Tsane, in the heart of the Kalahari Desert, about 300 miles (482.7 km.) north-west of Mafeking, and there we think that we have located an African population which may well provide us with the information in question. Every household owns cattle, goats, and sometimes poultry; in addition, there is plenty of game—springbok, wildebeest, etc.—which is trapped or shot. A good supply of meat, and usually a fair supply of milk, are thus available. Sufficient maize, kaffir corn, and beans are grown to satisfy requirements, at least in seasons of normal rainfall. For vegetables there is tsama, a species of wild melon that is extensively cultivated and eaten both fresh and dried. From the diet consumed it is understandable that the clinical state of the people, particularly the young, was found to be excellent. Furthermore, examination of samples of blood smears, sera, throat swabs, sputa, urine, and faeces provided no evidence of current or, in certain respects, of past infestations and infections. Although these people would appear to be almost ideal for furnishing the biochemical data required, it must be admitted that the rainfall is unreliable, and that droughts cause occasional shortages of certain foodstuffs. There is, however, an African police post at Tsane, the members of which, in addition to receiving their pay, are able to run their kraals and small farms; it is considered that the standard of the diet of such families is likely to be affected little or possibly not at all from seasonal shortages. This would also apply to the families of the larger cattle owners, of whom there are several.

It is our hope to return to the area and by careful inquiry and examination to select subjects (1) that have been very probably habituated to a good diet, and (2) that have lived in the region throughout their lives and thus have probably not suffered from, nor are suffering from, the infestations and infections so very common to Africans elsewhere. We are sanguine, therefore, of obtaining data of the type enumerated above, at least for children and young adults. Such knowledge should allow a start to be made in the assessment of the possible factors influencing the abnormalities listed at the beginning of this letter.

Our initial expedition was made possible by the South African Council for Scientific and Industrial Research, the South African Institute for Medical Research, and the medical authorities of Bechuanaland Protectorate, to whom we are deeply indebted, and with whose permission this letter is published.—We are, etc.,

A. R. P. WALKER.
B. T. SQUIRES.

Johannesburg.

Kwashiorkor in Ibadan

SIR,—During the past four years a large number of cases of kwashiorkor have been seen in Ibadan, Nigeria, and, although conforming to the general picture as painted by the Makerere team (October 11, p. 791 *et seq.*), the following points may be of interest.

Kwashiorkor is called by various names by the Yoruba people, and one of the commonest is "ela" or "licking," referring to the skin rash, which is thought to be due to worms in the body licking off the skin from within. Mild or "latent" kwashiorkor, associated with failure to gain weight, apathy, etc., is well recognized as a dangerous, though common, phase of growth in infancy. It is known as "owowe" or "falling (of the leaves)," which refers to the well-known sparseness of the hair.

The age distribution in Ibadan is fairly similar to that in Uganda. In 1950, of 44 cases treated, 64% occurred between the ages of 18 and 36 months. They did, however, appear to differ in that many were still not completely weaned from the breast when the disease developed, although it seems unlikely that they were receiving more than very little breast milk. In Ibadan, kwashiorkor is commonly found, at least in older infants, in association with infective gangrene of the mouth (cancrum oris), which may itself have a nutritional basis.

The less spectacular skin lesions remarked by the Makerere team were also common in Nigerian cases (that is, deep bleeding fissures behind the ears, etc.; grey circular "slumbering" ulcers). As regards the now classical "crazy pavement" rash, I agree that the emphasis should be, at least in severe cases, on the fact that it consists of a "raw" desquamation—large fine hyper-pigmented flakes peeling to leave a weeping, or at least very thin and pale, underlying skin. In Ibadan, as was noted by Brock and Autret, it is common for this rash to involve the whole body surface.

One cannot help wondering whether the roundworm should not have been mentioned in the discussion on the role of parasites in kwashiorkor. Some 90% or more of children in Ibadan are infected, and, as many hundreds of worms may be present in a single child, interference with protein absorption seems highly probable.—I am, etc.,

D. B. JELLIFFE.

Jamaica, B.W.I.

Education of the Epileptic Child

SIR,—Your leading article (October 11, p. 823) underlines a problem that has given concern to education and health authorities for some time, but the size of the problem is difficult to determine. Among the 400,000 children in London County Council schools a recent inquiry revealed 249 "epileptics." Of these, 166 are attending ordinary schools. This means that their treatment is adequate, and the community is ready to accept their occasional seizures, whether these are major fits, minor, or some equivalent. This figure of 249 children is probably too low, but the excess will consist of other children like these who are able to lead much the same kind of life as normal school-children, and who have not therefore been brought to the notice of the school physician. Of the remaining 83, 11 are in schools for the educationally subnormal, 12 are in schools for the physically handicapped, where attention is available for their more frequent fits and transport between home and school can be provided, 58 are in epileptic colony-schools, and two 5-year-olds are at home while the result of further treatment is observed.

The two greatest difficulties met with in the care of these children are to ensure effective treatment, and to persuade the community in which they live to accept them. The first means that the parents have to co-operate with the family doctor and with the hospital over what must seem a very long period, and the second means that teachers, school-fellows, and the parents of other children have to overcome any repugnance they may feel. The fear and other emotions aroused by a major fit in a companion are not easily dispelled, but in some schools that have faced this problem the most encouraging results have been obtained. If this attitude were general there might be no need for a special school for maladjusted epileptic children, for their acceptance by the community should reduce the amount of maladjustment, or, if maladjustment is sometimes part of the syndrome, then such children could be admitted to the existing special schools for maladjusted children. As such a Utopia has not yet arrived, it is perhaps necessary to consider the provision of some form of special education for the few children who cannot be accommodated in one or other of existing types of school.—I am, etc.,

London, S.E.21. DENIS PIRRIE.

Arterial Spasm in Limb after Venepuncture

SIR,—Whilst reading the article on "Arterial Spasm due to an Intravenous Infusion," by Dr. M. Sutton (October 18, p. 859), I was reminded of a much commoner phenomenon which receives little recognition in textbook or article. I am referring to arterial spasm in a limb following venepuncture, either for withdrawal of blood or for transfusion by a drip.

I first came across this phenomenon some years ago when I had visited a case with an obstetrical flying squad. I had used both arms for the drip, so that I was taking blood pressure on an arm which had had a previous venepuncture. The radial pulse was poor and the blood pressure was low, and it was some time before I realized that the pulse on the other arm and over the carotid was quite good, and that in fact the patient had already responded to transfusion. I have met this phenomenon several times since, and only the other day a dramatic demonstration of it was seen in my ward. A woman was admitted to hospital following an abortion with haemorrhage : during the course of treatment venepuncture had been made into both median basilic veins. I was called to see her because both radial pulses were weak, thready, and rapid, although one house-surgeon pointed out that the patient's face was red and florid whilst her hands were cold and blue. On further examination a bounding carotid pulse was found, which made it apparent that the weak radial pulse with the low blood-pressure recording on each arm was due to local arterial spasm. The patient was, in fact, not shocked, but toxic, for she had a raised temperature which caused the rapid pulse.

It is quite reasonable that this phenomenon should occur, for Ochsner (1940) has already described the reflex spasm that can occur in a limb following thrombosis in a vein. It is perhaps, therefore, not surprising that simple venepuncture should produce a similar spasm. It is important to realize that this can occur, for failure to recognize the true condition might lead to the continuance of transfusion long after the necessity for it has ceased. It is true that other signs and the patient's general condition should help to counteract the impression given by the falsely low blood-pressure recording on the arm which had undergone venepuncture, but, by the unwary, these additional guides might be overlooked.—I am, etc.,

Bristol. T. F. REDMAN.

REFERENCE

Ochsner, A., and De Bakey, M. (1940). *Arch. Surg. (Chicago)*, **40**, 208.

Severe Damage to Limb after Blood Transfusion

SIR,—Dr. M. Sutton's article (October 18, p. 859), recording a case of arterial spasm due to intravenous infusion, recalls a case in which severe damage to a limb followed a blood transfusion, and two further cases of minor circulatory impairment from the same cause.

Case 1.—A girl of 18 was admitted for an emergency appendicectomy. A pelvic abscess was drained nine days later. After an initial improvement the patient became increasingly toxic, intestinal obstruction developed, and it was decided to perform a laparotomy in an attempt to relieve her obstruction. The patient's general condition was poor, blood pressure 105/80, pulse 120, poor volume, temperature 100.6° F. (38.1° C.), face and extremities pale and cold. A saline intravenous drip was set up in the dorsum of the right hand, pending the arrival of blood. Thiopentone 0.25 g. and tubocurarine chloride 16 mg. were injected into the drip tubing, and after intubation the anaesthetic was continued with cyclopropane and oxygen.

The operation lasted one and a half hours, during which time the gut was freed of adhesions and 2½ in. (6.35 cm.) of intestine resected and a large abscess in the right flank drained. After three-quarters of an hour the patient's blood pressure became unrecordable. The intravenous saline was changed to blood, the table placed in the Trendelenburg position, the anaesthetic discontinued, and oxygen alone administered. At the end of the operation the systolic blood pressure was 80, pulse 150, and 2½ pints (1.7 l.) of blood had been transfused.

Soon after the blood transfusion commenced the right hand and distal two-thirds of the forearm became a mottled purple colour. The left hand was also blue and cold and the peripheral circulation was extremely poor. The radial pulse was perceptible in both wrists, but was weaker on the right. On return to the ward, warmth was applied to the arm. In all, 4 pints (2.27 l.) of blood were transfused and the drip was continued with dextrose-saline for 48 hours.

The patient's peripheral circulation never improved after operation and death occurred on the fifth post-operative day. The circulation was always worse in the right arm, which remained blue and cold and after 48 hours began to swell, when the drip was discontinued. The radial pulse at this stage was just perceptible, but disappeared on the right side as the swelling increased. For 24 hours before death it was impossible to feel a pulse in either wrist. The right hand and distal third of the forearm progressed to frank gangrene with bleb formation.

Case 2.—A middle-aged woman was admitted with a ruptured ectopic pregnancy and severe intra-abdominal bleeding. Her pulse could scarcely be felt, her blood pressure was unrecordable, and she was semiconscious. An intravenous blood transfusion was set up in a vein on the flexor surface of the left wrist—the only vein visible—and as soon as her systolic blood pressure reached 90 mm. laparotomy was performed. The operation lasted 30 minutes, and during this time the left hand and distal half of the forearm assumed a purplish mottled appearance identical with Case 1. The radial pulse was present, but the volume was diminished compared with the right. Once the bleeding vessel had been ligated and the peritoneum closed the patient's condition rapidly improved and the blood pressure rose to 120/80. The circulation in the left arm improved fairly quickly, and it became warm and pink again while the drip continued.

Case 3.—A woman, aged 65, was undergoing an operation for abdomino-perineal resection of rectum. During the operation her

blood pressure fell from 140/70 to 110/70. An intravenous blood transfusion was given throughout the operation, which lasted an hour, into a vein on the dorsum of the right hand which ran superficial to the space between the fourth and fifth metacarpals. At the end of the operation the fourth and fifth fingers were found to be cold and purple in colour, the tips of the fingers being dead white. Warmth was applied to the hand in the ward, and the drip continued for another hour, without improvement in the appearance of the two fingers. The drip was changed to a proximal vein in the other arm, with immediate return of circulation in the right hand.

In Case 1 the patient's peripheral circulation was minimal, and the diminution caused by the cold blood entering the limb was sufficient to precipitate gangrene. Case 2 might have ended in the same way if the transfusion had been continued long enough and if the patient's general condition had not improved.

These cases are in no way comparable to that of Dr. Sutton's, in which the stimulus causing spasm was an intravenous needle lying in close proximity to the arterial wall and acting as an irritating foreign body. In the above cases the stimulus was that of cold acting upon a circulation which was already impaired. But they serve to draw attention to the danger of using peripheral veins to transfuse blood, for long periods, in patients whose general condition is poor.—I am, etc.,

Isleworth, Middlesex. A. B. VAUGHAN.

Lumbar Intervertebral Disk Protrusion

SIR,—In view of recent correspondence about "painful back" I believe Dr. D. M. Graham-Service (October 18, p. 882) may be on the right track. I am with him in condemning back supports: it seems to me there can never be support of the back when the belt is partly enveloping the movable abdomen. All the same, I feel he has missed the point in endeavouring to replace bony structures by manipulation, and even when he has done so I fail to see how he can be certain that these have been replaced micro-accurately, if I may use the term. I have no doubt he is right to try to correct the posture, but I feel he is wrong in directing treatment to bones and joints rather than to muscle groups. If for any reason there is postural alteration of bones or of the joints related to the back, it seems quite obvious that muscle groups must then take on the permanent job of trying to hold the pre-injury posture.

It would seem, therefore, that we have a condition of chronic muscle spasm together with an associated ache. Local analgesia benefits most of these cases more than anything else except rest in bed, but with neither treatment do we get permanent relief. Certain surgeons seem to be showing some advance in their ideas of lengthening the tendo achillis, but they do not seem to realize that by so doing they allow the individual to take his weight more on the tarsus than on the heel. I have found great relief in most cases by a much simpler method—namely, by raising the heel of the man's shoes ¼ in. (0.6 cm.) or more.

For some unfathomable reason pitching the balance forward tends to relief of symptoms, and I think that here is a great opportunity for someone with ample time and facilities to investigate this approach. On the whole this gives more permanent relief than any other treatment I have investigated.—I am, etc.,

London, S.W.1. VINCENT HYSLOP.

SIR,—I cannot let Dr. D. M. Graham-Service's letter (October 18, p. 882) pass without comment, because it contains two statements which do disservice to our patients. In discussing diagnosis Dr. Graham-Service says that "apart from these two methods (i.e., operation or myelography) I do not think that an absolutely definite diagnosis of disk protrusion can be made." He goes on to suggest other causes for pain, and continues: "Here I agree with Mr. Henderson that because the condition is essentially subjective it is difficult to assess the results of conservative treatment." It would appear from these two statements that the criteria on which the diagnosis is made by these two gentlemen are inadequate.

I believe it is true to say that no surgeon with any experience would operate on, or treat by any other method, a patient thought to be suffering from a disk protrusion unless there were ample objective signs that this was the cause of the symptoms. The first set of signs are those relating to the spine, and concern its posture, its range of movement, and the presence or absence of tenderness. In their absence one seeks for some other cause of the sciatica. The second set of objective signs relate to the lumbo-sacral plexus of nerves. The most important are the alteration of a reflex or of skin sensation. I do not forget the importance of *x* rays and examination of the cerebrospinal fluid, or the great stress to be laid on a detailed history, or the assessment of the patient's emotional state and domestic, social, and industrial background. I take these for granted.

It is possible for a patient to have pain referred down a leg, but in the absence of signs indicating that one or more nerve roots are involved there must be some other cause than that of a protruded intervertebral disk, or any other lesion—such as an abscess or tumour—capable of involving the nerve root. It must, I think, be the experience of every surgeon that subjective sciatica has been caused by lesions of joints and in particular of the sacro-iliac joint; while it has recently been reported that osteoid osteoma, either of the vertebral body or of the neck of the femur, has been operated on mistakenly as cases of protruded intervertebral disks.

Finally, I have often been struck by the spelling of "disk" in your *Journal*. According to my anatomy book it should be spelt "disc," and according to my dictionary a "disk" is a flat circular surface, and a "disc" is a flat circular object. There is not the slightest shadow of doubt that the disks on which I have operated were objects and not surfaces.—I am, etc.,

Manchester, 3. W. SAYLE-CREER.

*** *The Shorter Oxford English Dictionary* remarks: "The better spelling is disk."—ED., *B.M.J.*

Gluten in Adult Coeliac Disease and Idiopathic Steatorrhoea

SIR,—The new light which has been cast upon the problem of coeliac disease by Dicke[1] and others in Holland, and later confirmed by the Birmingham workers, Anderson *et al.*,[2] has stimulated renewed interest in the problem of the malabsorption syndrome.

We have been interested to learn the effect of gluten on adults suffering from the malabsorption syndrome, for we have recently had in our wards two females, aged 42 and 30, who gave a history of diarrhoea in childhood, and are now of the petite size which may be found in those whose growth has been hampered by coeliac disease. They have been proved cases of fat malabsorption as the result of repeated fat balance studies. It seemed to us that the same improvement should occur in these patients when wheat flour was removed from the diet as occurs in children. They were therefore placed on a diet free of wheat flour. Neither of the patients was suffering from diarrhoea at the time, and this diet made no alteration to their bowel habit. Fifteen grammes per day of gluten, which would represent the content of about ½ lb. of bread, was then added to the same diet for a period of six days. The patients were unwilling to continue with the diet for longer. In neither was there any loosening of the bowels during this period. The fat absorption figures during six days on a gluten-free fat balance diet, and again during six days on the same diet with added gluten, were respectively 81.8%:81.3% for one patient and 84%:88.5% for the other. Both these patients had been on a maintenance dose of pteroylglutamic acid for some time, and this was continued during the experiment.

A third case of coeliac disease, 17 years of age, had had symptoms of the disease since the age of 11 months, and had been in hospital many times subsequently. We gave her gluten 15 g. to take every day at home, in addition to her usual food. After six weeks of this she reported that

she had in no way been upset by the gluten, and indeed had gained a little weight. Two adults suffering from idiopathic steatorrhoea showed no clinical change when given a wheat-gluten-free diet for 11 and for 21 days respectively, nor when gluten was added to the same diet for a similar period. Fat-balance studies showed absorption of 48.2% and 45% respectively by the two patients on gluten-free diet, and 60% and 53% respectively when gluten was added to the diet. Five other patients suffering from the malabsorption syndrome who were being maintained on the usual low fat, restricted carbohydrate, sprue diet were given gluten 15 g. daily, to be taken with their food for six days. In no cases did this addition cause any deterioration in the bowel habit, or discomfort.

If it is believed that wheat gluten has a deleterious effect in the adult or adolescent case of coeliac disease or in idiopathic steatorrhoea, and that this effect is due to an idiosyncrasy or allergy, it would be expected that some sign of improvement would be noted when the wheat gluten was removed from the diet, but this was not found to be the case. If the effects were due to a toxic action, further deterioration would be expected when an excess of gluten was given, but this did not appear to be so. Indeed, no evidence was obtained from this investigation to suggest that gluten was playing any part in the causation of the fat malabsorption syndrome. It must be noted, however, that the test periods during which gluten was deleted or added to the diet were usually of short duration (six days) except in three cases, and the possibility exists that different results might have been produced if all the experiments had been continued for several weeks.—I am, etc.,

Edinburgh. H. T. SWAN.

REFERENCES

1 "Coeliakie," Utrecht, 1950, M.D. thesis.
2 *Lancet*, 1952, 1, 836.

Asthma in Childhood

SIR,—I would like to enter into verbal combat with Dr. Cyril Josephs (October 18, p. 881) concerning bronchial asthma in children. The most convenient way of viewing this condition is to divide it into three groups; (1) true allergic asthma (I hope to demonstrate to your correspondent that such a condition does exist), (2) asthma associated with psychological disorders, and (3) asthma secondary to other lung conditions such as bronchitis and sometimes bronchiectasis.

From our practice, which is chiefly industrial, I took 10 children, all of whom suffered from severe recurrent attacks of bronchial asthma, and carried out dermal sensitization tests on them. Seven showed reaction to a specific allergen, and in each one of these seven cases a positive family history of asthma or an associated allergic disorder was elicited. In four of the subjects eczema, flexural in site, was also present. Of the remaining three cases, those not reacting to the tests, no positive family history was obtained. In two of these a strong psychological element was present, and in the remaining case the little boy was a sufferer from chronic bronchitis.

The cases showing a sensitivity were all cured with courses of desensitization with the particular allergen and have been followed up for three years. The associated eczema cleared up in all but one case. From the three non-allergic subjects I took a control and administered a course of normal saline injections without effect.

I found the provoking substances were all of the inhalation group, and I have not tried to eliminate them environmentally. Of course the series is small, which it really must be in general practice, but it has convinced me at least that allergic asthma does exist and may respond to such type of treatment as has been discussed. I quite agree with Dr. Josephs that a psychological element may be found in many sufferers from the condition, but these are surely distinct from the true allergic phenomena, though sometimes they may co-exist.—I am, etc.,

Derby. BERNARD JACOBSON.

Perseverance in Artificial Respiration

SIR,—Dr. F. C. Eve (October 18, p. 879) asks for details of cases of long-continued artificial respiration. We can supply at least one authenticated case. The late Mr. W. A. S. Calder, of Chance & Hunt, Ltd., was tireless in preaching the value of continued effort, especially in connexion with hydrogen sulphide, and in November, 1934, the Association of British Chemical Manufacturers issued a special Safety Circular No. 70, from which is taken the following:

. . . "particulars of evidence which has led him to conclude, from his extensive wartime experience of cases of gassing by hydrogen sulphide, that by continuing efforts of resuscitation, long after all reasonable hope might appear to have been abandoned, fatalities may almost invariably be avoided. He informs us that there was a very large number of men who were rendered completely unconscious by this gas, yet there was not a single fatality among them, although in some cases it required many hours of hard work to bring a man round."

An account is then given of a case on June 9, 1910, when a worker was overcome by hydrogen sulphide in a canal boat and lay unconscious for probably half an hour before he was discovered. After Schaefer artificial respiration for some three hours on the canal bank, this treatment was supplemented by oxygen. Mr. Calder went on to say:

"After several hours' further treatment, the man revived and, as soon as possible, hot coffee was given; he was hauled to his feet and made to walk about with a man on each side holding him up. He gradually recovered, regaining the use of his limbs, and was then wrapped in blankets and sent to hospital. He returned to work on July 16. Apparently the accident had no permanent ill effects, although he was described as a man who was particularly susceptible to asthma and bronchitis previous to his accident."

The concentration was considered to be at least 1% of hydrogen sulphide. The doctor in attendance reveals from his diary: "I was called at 7.30 a.m. and stayed until 8.30, then I had to leave, but came again at 10 a.m. and remained with him to 1 p.m., when he began to come round. I left then, but was back at 2.30, and at 3.15 he was removed to hospital. He was entirely unconscious for over six hours, and I am sure that it was only the continuous application of oxygen that saved him."

Mr. Calder also reported that on another occasion seven men became unconscious after an escape of gases containing 35% of hydrogen sulphide. In this case the men were all brought round without the use of oxygen. The worst of these cases took "several hours' treatment, yet the man some years afterwards went on active service in 1914."

The Safety Circular ends by remarking that, although the above experience is confined to the effects of hydrogen sulphide, it suggests that it would be worth while in cases of poisoning by other gases to continue artificial respiration long after it would seem to be hopeless. It is realized, of course, that these results are partly due to the peculiar action of hydrogen sulphide, but they do seem to support the value of long-continued artificial respiration.—I am, etc.,

Association of British Chemical Manufacturers, London, W.1. ALLAN J. HOLDEN.

The Harveian Oration

SIR,—While of course agreeing with Lord Moran in wanting "to purge the practice of medicine of all those elements of humbug," there is a very great danger indeed in making it unnecessary to win the favour of the patient. May not the pendulum swing the other way and the patient's confidence be lost? One hears so frequently: "I was told nothing," "I see a different doctor each time," "It means waiting so long, so many tests and examinations and then being told nothing," "I never see my own doctor, always an assistant," etc.

Indeed, the last sentence of the Oration, as reported, might have been in large block letters, for the human touch is fast vanishing from the Welfare State. The sentence was as follows: "The danger in this was that in the cultivation of medicine as a science the physician might neglect medicine as an art."—I am, etc.,

London, N.W.8. HENRY CHURCHILL.

Dangers of Atropine in Cases of Traumatic Iridodialysis

SIR,—During the Italian campaign B. W. Rycroft (Allied Force Headquarters, Ophthalmic Bulletin, C.M.F.) insisted that immediate mydriatics in cases of traumatic hyphaema due to contusio oculi were contraindicated, and that in severe cases the correct treatment was the avoidance of all medication by drops, complete rest, and "double padding" for 48 hours. The following case illustrates the danger of producing a massive haemorrhage in cases of rupture of the iris by the instillation of a mydriatic and cycloplegic even for examination purposes.

H.G., a male aged 20 years, fell supine and hit his left eye on an object lying upon the ground. When examined the following day he showed a traumatic dialysis at 3 o'clock to the extent of 2 mm. without haemorrhage. There was a superficial scar of 2 mm. lying transversely across the limbus in the same situation, faintly absorbing fluorescein but not penetrative. 5 mm. to the temporal side was a sub-conjunctival ecchymosis. Homatropine was instilled for ophthalmoscopic and slit-lamp examination, but no foreign body was found, although the wounds suggested probable penetration by a thorn or similar object through the limbus. The fundus showed marked concussive changes in the lower temporal quadrant, with small retinal haemorrhages, and the vision was 3/60.

The patient was admitted and the following morning brought to the theatre after the instillation of gutt. atropin. 1% for examination and possible reflection of the conjunctiva to search for a problematical splinter of wood. It was decided not to conduct such a procedure and the patient was returned to bed. Thirty-six hours later the patient developed a large hyphaema and a presumed vitreous haemorrhage. The hyphaema had its obvious origin at the site of the dialysis. All local medication, except ice packs, was stopped and the hyphaema cleared within seven days, but the vitreous was full of blood. The vitreous cleared gradually, and five weeks later it is possible to observe remaining blood clot adherent to the ciliary body at the site of the iridodialysis. Vision is 6/12 and the fundal reflex and vessels are visible through the blood-stained vitreous. There is now a puckered scar of the iris in the midzone in the 3 o'clock meridian, and the iridodialysis has closed except for two tiny "holes" at the angle.

It would appear that the two obvious explanations for the haemorrhage are (1) reactionary, which might have occurred irrespective of the exhibition of atropine, and (2) the disturbance of clot in a vessel due to the exhibition of atropine for examination purposes.—I am, etc.,

Leamington Spa. MAURICE W. SMITH.

Nervous Signs in Sarcoidosis

SIR,—I have read with considerable interest the paper on "Nervous Signs in Sarcoidosis" by Dr. M. Jefferson (October 25, p. 916). I have been interested in the subject since making a review of it in 1948 (Colover, J., *Brain*, 1948, **71**, 451), when I collected 115 such cases from the literature.

Any discussion of this subject is incomplete without reference to those cases of meningo-encephalitis which show symptoms and signs of raised intracranial pressure, as they are usually diagnosed as cases of cerebral tumour or, alternatively, no diagnosis is made during life. These cases may have space-occupying granulomata, or may have a posterior fossa arachnoiditis. In the latter case, the immediate prognosis may be improved after posterior fossa exploration and opening up the cerebrospinal pathway. Possibly some of these cases in the past were regarded as cases of "pseudotumour," as they presented with headache, vomiting, papilloedema, etc. A number of them have now been reported, and usually the signs of sarcoidosis elsewhere are minimal and the diagnosis has only been made at necropsy. However, in view of the typical sarcoid reaction in the meninges and from the evidence in cases which have been examined post mortem, there can be little doubt about their correct classification. During life the diagnosis may only be arrived at if biopsy is performed on the arachnoid in cases which have a posterior fossa exploration.

Regarding the symptoms of the patients with multiple neuritis, I would like to draw attention to the sensation, described by the first patient in Dr. Jefferson's paper, of patches of skin feeling "cold" or "frozen." It is noteworthy that a number of these patients use this identical phrase in describing their symptoms, and it may well be a special feature of this form of neuritis. The pathology of it is little known, except that the peripheral nerves may show infiltration with sarcoid tissue as described and beautifully illustrated in 1908 in the paper by Mazza (*Arch. Derm. Syph., Wien*, **91**, 57).—I am, etc.,

London, W.2. J. COLOVER.

Acetylcholine in Anxiety States

SIR,—The reply on "Acetylcholine in Anxiety States" ("Any Questions?" August 9, p. 349) has come to our attention only now. We hope, however, that you will find it possible to accept the following somewhat belated comment on two important points.

Whilst we fully agree that "in nearly all anxiety states the disturbance is of the autonomic system as a whole, and though sympathetic overaction may be dominant, some overaction of the parasympathetic system will be seen in individual symptoms," it seems to us that the necessary conclusions from this are not drawn—namely, sedation of either both branches of the autonomic nervous system, or, more specifically, sympathetic sedation. Further, the use of acetylcholine as an antagonist to adrenaline seems a rather roundabout way to achieve an equilibrium, acetylcholine being the stimulant of the parasympathetic and not a sedative of the sympathetic. Although there may be no drug which is solely an antagonist to adrenaline, there are several which come nearer this description than acetylcholine. "Hydergine," and its component dihydroergocornine (D.H.O. 180), have been shown in our investigations on anxiety states[1] to possess a powerful adrenolytic effect in man. We have also investigated[2] the influence of "bellergal," which acts as a sedative of the parasympathetic as well as of the sympathetic and the central nervous system, on anxiety states.

In previous publications[3,4] we have shown that anxiety states in tense individuals are usually accompanied by peripheral vasoconstriction, as evidenced by plethysmographical findings; in the hysterical or neurasthenic patients, on the other hand, we have observed peripheral vasodilatation. Our recent investigations have demonstrated that these tense anxiety states with sympatheticotonic predominance—that is, peripheral vasoconstriction—respond to treatment with the sympathicolytic and adrenolytic drugs used (hydergine and dihydroergocornine) and also to treatment with bellergal. Not only was subjective improvement achieved, but simultaneously a marked improvement or normalization of the plethysmographic pattern also ensued. Thus, it does not seem necessary to counteract the effect of adrenaline, or rather of sympathetic overstimulation, by stimulation of the parasympathetic with acetylcholine; the logical course—that is, sedation of the sympathetic or of the entire autonomic nervous system—also seems to produce the desired effect.—I am, etc.,

Stellenbosch, S. Africa. A. B. VAN DER MERWE.

REFERENCES

1 Goetz, R. H., and Katz, A. (1949). *Lancet*, **1**, 560.
2 Paper read at the 38th Congress of the S. African Medical Association, Johannesburg, September, 1952; to be published in full shortly in the *S. Afr. med. J*
3 Van der Merwe, A. B., and Theron, P. A. (1947). *J. gen. Psychol.*, **37**, 109.
4 —— (1948). *Psychosom. Med.*, **10**, 347.

Pathologists' Opinions

SIR,—There appears to be an increasing and regrettable tendency for pathologists, called to give evidence at inquests, being led to give opinions on matters outside their specialty. These opinions are frequently reported in the Press, so that the public receive unanswered and often faulty ideas about the hospitals or medical personnel concerned.

A recent example was in the *Daily Telegraph* of October 31, where a Home Office pathologist was reported

to have said: "I don't think there was enough done here. I don't think the fracture should have occurred. That was bad nursing. I don't think the condition of constipation should have occurred. That was bad nursing and bad doctoring."

It is pertinent to inquire what clinical experience the average pathologist has to enable him to give opinions on nursing or treatment problems. Surely the pathologist at an inquest should confine himself to a pathological report on the body and an opinion on the cause of death. If the coroner wishes for opinions on the correctness of treatment carried out before death he should call other and suitably qualified witnesses.—I am, etc.,

Watford. ROBERT C. TAYLOR.

The Humby Knife in Removal of Burn Sloughs

SIR,—Mr. A. J. Evans's admirable note (November 1, p. 979) on the value of the Humby knife for the easy and quick removal of extensive burn sloughs invites comment. My first is to express full agreement with those who hold that the Humby knife (designed by Mr. Graham Humby some 20 years ago when he was a junior dresser to Sir Heneage Ogilvie) is still the most generally useful grafting instrument in surgery to-day. I can confirm its value as a means for removal of skin sloughs quickly and with minimum blood loss; but I prefer for this purpose the electric dermatome when this is available (until recently there were only two in this country—one at Basingstoke and one at Birmingham). The electric dermatome removes skin sloughs even more quickly and with less effort; but neither the Humby knife nor the electric dermatome is practicable for burns of the face or hands, where we await an efficient and safe chemical or enzymic agent—the bloody method of scissors and knife must still be used in the early removal of burn sloughs.

Blood loss is a major difficulty to the removal of sloughs in extensive burns at the optimum time—that is, at the earliest moment that the procedure is safe and the assessment of depth certain. I mention this to make the point that hypotensive drugs, carefully and skilfully given to these ill patients, can be of critical value in the removal of extensive sloughs early in the second week, with a minimum of external blood loss and of graft loss due to haematoma. —I am, etc.,

London, W.1. PATRICK CLARKSON.

Is Boxing Safe for Schoolboys?

SIR,—To my surprise, the reply to the question "Is boxing safe for schoolboys?" (October 25, p. 952) made no reference to the deviate septum, and this I consider is the most common form of permanent injury, the danger of which is the sequela of chronic sinusitis. Could one of the medical officers in charge of boys' boarding schools give us any light on how many boys arrive at 13 with perfectly good noses, and leave at 17 and over with deviate septums?

I believe it is officially established that Great Britain has the doubtful honour of having more chronic sinusitis than any other country. She also has the honour of being foremost in promoting boxing at boys' schools.—I am, etc.,

Harrow-on-the-Hill. H. CRICHTON-MILLER.

Ichthyosis and Hypnosis

SIR,—Dr. A. A. Mason's successful treatment of a case of congenital ichthyosis by means of hypnosis (August 23, p. 422) may well open up a new province in pathology and therapeutics. It is the congenital origin of the symptoms that gives this case its deep significance. The case is unlike anything previously recorded, and in seeking for a hypothetical explanation it may be useful to consider a condition which, though of widely different nature, is cognate in certain of its aspects. Such a condition is that designated by Babinski as "physiopathic paralysis of the hand." Though rare in civilian life, these cases were numerous during the 1914–18 war. As the result of a slight wound of the upper extremity the patient developed a hysterical paresis of the hand which was associated with sweating of the palm, local circulatory changes, and severe trophic changes in the skin and nails of the affected hand. These cases were much discussed, and were generally regarded as of psychological origin. With improvement in the mental condition, the paresis and the circulatory and trophic changes disappeared (Abercrombie, R. G., *British Medical Journal*, 1920, **1**, 764). In these instances a powerful morbid impulse, arising at the level of consciousness, had brought about a disturbance of function in the circulatory and trophic centres, giving rise to pathological changes in the skin of the hand.

In Dr. Mason's case the morbid changes in the skin were of congenital origin, and were apparently to be ascribed to an obscure developmental defect, perhaps in the development of the synapses, slight in grade, but sufficient to upset the balance of neural control with a consequent disturbance of function of the circulatory and trophic centres associated with gross changes in the skin. As the result of hypnotic treatment, a powerful reinforcement was given to the controlling influence of the higher centres, thus compensating the congenital defect and bringing a return to normal trophic conditions and a cessation of the pathological process of the skin.

Although so dissimilar, the cases of physiopathic paralysis and Dr. Mason's case of ichthyosis both illustrate the paramount influence sometimes exercised by the highest centres upon the lower centres governing circulatory, secretory, and trophic effects.—I am, etc.,

Sheffield. R. G. ABERCROMBIE.

SIR,—Dr. A. A. Mason and I, it appears, have been trapped by a confusing nomenclature—as Dr. Ray Bettley has pointed out (November 1, p. 996). Dr. Mason's *congenital* ichthyosis and Professor H. A. Magnus's ichthyosis *congenita* in the text of Dr. Mason's original article caught my eye, to the exclusion of ichthyosiform erythrodermia of Brocq in the heavy block capitals at the head of his original article, and also on the outer cover of that number of the *Journal*. I apologize, and confess that I had never heard of Brocq's rare disease; but it was not until Dr. Mason said in his last letter that he was tired of reiterating that ichthyosiform phrase that I looked to see if he had ever used it. It was only to be found in that original heading which Dr. Mason himself had misquoted as "The Treatment of Ichthyosis by Hypnotism"—leaving poor M. Brocq out of it.

It seems that the ichthyosis so common in an allergy clinic should now be called ichthyosis simplex and certainly *not* ichthyosis congenita, though nearly all the cases seen there are declared to be congenital by patients or parents—who should know. I therefore submit that ichthyosis congenita is not a sufficient label for the rare and monstrous form of Brocq's disease. (I have, by the way, seen a presumably ichthyosis simplex case malformed at least up to crocodile point.)

As for the twists of meaning given to "allergy," I suggest that the able brains who are trying to make a coherent picture of it are like people trying to fit together in one picture the very imperfect collection of pieces from several different jigsaw puzzles all mixed together in one bag. Amidst the welter of contradictory facts and nebulous definitions there emerges, I think, the suggestion of at least one coherent whole—"The Allergic Disorders," Coca's "Atopy," my "Toxic Idiopathies." It is to that still fragmentary picture that I assign ichthyosis simplex of the allergy and dermatology clinics. My simple syllogism runs: (1) Ichthyosis (simplex) is a toxic idiopathy; (2) all toxic idiopathies are affected by the emotions and mental attitudes. Therefore I am not so very surprised to find that ichthyosis (simplex) is affected by hypnotic suggestion.—I am, etc.,

London, W.1. JOHN FREEMAN.

Period of Gestation

SIR,—Most valuable and accurate information could be given on this subject by married couples where both husband and wife are doctors. We are such a couple, and over the first seventeen years of our married life three births occurred. The first pregnancy was associated with 255 days of amenorrhoea; the second lasted 257 days from the actual day of fertilization, as did the third. At the birth of the first child, we assumed that he was premature in spite of his normal size and normal length of finger-nails. When the second child appeared after 257 days we rejected the idea of prematurity, especially as this child weighed 11 lb. (4.95 kg.).

The maternal menstrual cycle recurs every 24 days with remarkable regularity, and we thought that this shortened intermenstrual time might influence the gestation time to be shorter. On this basis we confidently and correctly predicted the approximate birthday of our third child.

Dr. S. H. Waddy, in his interesting letter (May 24, p. 1132) is thinking along similar lines, and he suggests that a pregnancy lasts ten times the mother's intermenstrual period. In our case, although there is such a tendency, the total gestation time from actual date of conception is more than $10 \times 24 = 240$ days; it is 257 days.

Possibly it is not only maternal factors that influence gestation time; the foetus is born when it is mature, and its rate of attainment of maturity may be inherited from both parents and be a compromise between the two. For example, every poultry farmer who crosses a female Aylesbury duck with a Muscovy drake knows that the resulting egg looks exactly like an Aylesbury egg, but the hybrid emerges at 31 days—a compromise between the respective periods of incubation of 28 days in the case of the Aylesbury duck and 35 days in the case of the Muscovy.

On the basis of our limited observation it would be foolish to dogmatize. We suggest, however, that some future investigation such as the Birmingham series should be analysed along lines to discover whether the gestation time is $10 \times k$, where k is a compromise between the intermenstrual time of the mother and the intermenstrual time of the females on the paternal side.—We are, etc.,

K. JOYCE MULVANY.
BERNARD GOLDSTONE.

East London, South Africa.

Perforation of Small Intestine

SIR,—Reading Mr. Hilary Wade's article (October 25, p. 922) on perforation of the small intestine reminded me of a similar case treated here last year.

A married girl of 26 was admitted with a 24-hour history of abdominal pain, which had moved from epigastrium to right iliac fossa. She complained of nausea but no vomiting. She was also suffering from thyrotoxicosis. A diagnosis of acute appendicitis was made. At operation a Meckel's diverticulum was found to be present, the apex of which had been perforated by a bristle lying partly in the diverticulum and partly in the peritoneal cavity, with an area of surrounding inflammation. The diverticulum was removed. The bristle was the size and shape of those used in the manufacture of tooth brushes.—I am, etc.,

J. B. BINKS.

Great Yarmouth.

An Obstetric Thimble

SIR,—In 1934 I published a very brief article, "A Simple Device for Rupturing Membranes" (*Amer. J. Obstet. Gynec.*, 1934, 27, 273), in which I suggested a spiked thimble for rupturing the foetal membranes. The thimble idea occurred to me while reading, in one of my grandfather's medical books, of the custom of the early accoucheurs to employ a sharpened finger-nail to rupture the membranes. Modern rubber gloves prevent the use of the finger-nail, but it occurred to me that a thimble with a raised pointed sector could be substituted.

This second report is to describe more fully my conception of an obstetric thimble and also to give a technique for using it. Any handyman can, with a jeweller's saw and file, make the device. Two cuts are made in the end of a silver thimble, these intersecting in or near the centre and at slightly more than a right angle. The sector so delineated is then slightly raised and the rough edges are polished off, preserving the point. A small hole is drilled in the base to which a stout nylon cord can be attached for retrieving the instrument in case it should slip off—an accident which rarely happens. Obviously, the foregoing method is by no means the only one of making a point or spike on the end of a thimble. Instrument-makers may suggest improvements which might simplify manufacture. The method I have suggested, however, seems safe and effective.

While some doctors have employed the obstetric thimble for initiating labour, I personally do not now recommend it for this purpose. I advise that the thimble be used only during the second stage of labour, when the cervix is fully dilated and tough membranes seem to be delaying the further progress.

The technique recommended is as follows: The sterilized thimble with cord attached is placed firmly over the tip of the first finger of the examining hand. The point of the thimble is towards the palm. The middle finger of the same hand is placed behind the first finger to protect the point from doing any injury to the soft parts. Previous examination having shown the cervix to be fully dilated, the head rotated and flexed, and no reason for a delay in labour, except tough membranes, the fingers are inserted in the vagina as for examination.

The middle finger being used for palpation, it is slightly flexed on encountering the membranes and a scratching movement is made with the first finger while the thimble is in contact with the membranes (between pains). The membranes are easily ruptured, allowing the escape of amniotic fluid. The technique is very easy and the danger to mother and child minimal. Of course, one should not mistake the buttocks, scalp, or face for unruptured membranes.

A great deal of obstetrics is still, of necessity, done in the home. Therefore an instrument which can be used by touch while the patient is in her bed has advantages. The obstetric thimble can be characterized as one of the less deadly of obstetrical instruments. Ease of technique should, however, not lead to unnecessary tinkering with the normal process of labour.—I am, etc.,

ROBERT P. LITTLE.

Quebec.

A Syringe Label

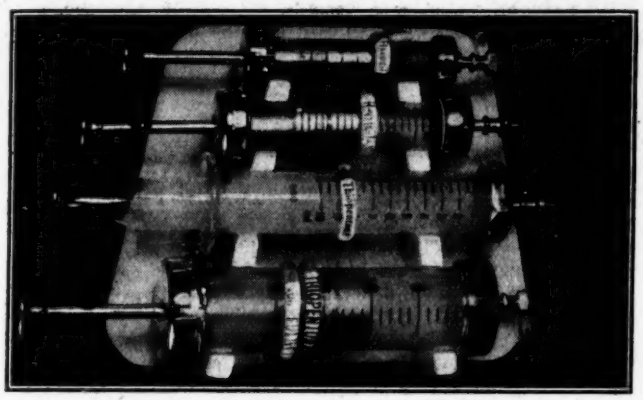
SIR,—Modern anaesthesia is typified by the multiplicity of drugs used. The large number of syringes which litter the anaesthetic trolley is mute evidence of this. The harassed anaesthetist is faced with watching the colour of the patient, his pulse and respiratory rates, blood pressure, general condition, and also four flowmeters, a rebreathing bag, and the contents of two or three syringes. The result of some confusion with the latter difficulty was that a search was made for a simple method of labelling the contents of a syringe.

The illustrated syringe-label clip was designed and made by the Senior Anaesthetic Technician of the Queen Victoria Hospital, East Grinstead, Mr. Cyril Jones. It is simple, cheap, and effective, and takes very little time to make.

The material is "perspex," and strips ¼ in. (6 mm.) wide are sawn off a sheet ⅛ in. thick. These strips are then cut up into varying lengths, the length depending upon the size of syringe it is intended to label. The clip encircles about three-quarters of the circumference of the syringe, and some approximate lengths are 20 ml. syringe, 2½ in. (6.5 cm.); 10 ml. syringe, 1¾ in. (4.5 cm.); 5 ml. syringe, 1½ in. (4 cm.); 2 ml. syringe, 1¼ in. (3 cm.).

After strips of the appropriate size are cut they are labelled. The label can be typed, but better than this are the printed headings found in the literature sent out by the drug houses.

The back of the perspex strip is moistened with a drop of chloroform, which is a solvent for perspex, and the label, which has previously been cut to size, is pressed into the softened perspex and left to dry. The back of the label is then coated with a varnish to render it waterproof. Mr. Jones uses a varnish



of perspex shavings dissolved in chloroform. Waterproofing the label is essential to prevent its becoming wet and torn, as many syringes are not absolutely dry when used.

The strip is then warmed until it softens, and bent round a syringe or any tube of a size equal to the syringe it is intended to label (test-tubes are very satisfactory). Very little heat is required, the perspex being rapidly flamed back and forth in a small bunsen flame. After bending round the tube it is plunged into cold water and it immediately becomes hard again. The clip can now be polished if required or used right away. Coloured perspex strips might be preferred by some, and are prepared in exactly the same way. The tensile strength of the perspex is considerable, and makes the ring a strong and effective spring clip.

A refinement of these clips may be obtained by chamfering, and then polishing, two edges, thus converting the cross section of the perspex from being square to convex. This has the effect of creating a convex lens in front of the printing and magnifies it considerably. The clips shown in the photograph were treated in this fashion.

These clips were demonstrated on October 4 at a meeting of the Society of Anaesthetists of the South-west Metropolitan Region, where they created much interest and received high praise.—I am, etc.,

East Grinstead, Sussex. A. A. MASON.

"Et all., etcc."

SIR,—While agreeing with Professor J. W. Howie's conclusion (October 18, p. 883), which is that "*et all.*" is nonsense, I can hardly congratulate him on the analogy he has chosen to prove his point. Surely "etc." stands, as it always stood, for *et cetera*, which was, and remains, plural. There can thus be no need for doubling the c any more than for doubling the l of "*et al*," which means *et alia* or *et alii*. Incidentally, this is a valid reason for supporting Professor Howie's contention, accepted now by most editors, that "*et al.*" should never be used when there is only a single co-author. On the other hand, the abbreviation "p." stands for a singular word, "page," and the use of "pp." for more than one page is logical as well as traditional, though typographically unpleasant to some people.

The choice would appear to be between, on the one hand, the italics of "*et al.*," with economy of space, and, on the other, the saving in setting of "and others" at some typographical extravagance.—I am, etc.,

London, N.W.3. A. L. BACHARACH.

Scalpel for Removal of Sutures

SIR,—Patients have a quite morbid apprehension of "having the stitches taken out." There is no doubt that when sutures have begun to cut into a wound the pressure of the blade of a pair of scissors under the suture does cause tension and pain.

Some years ago I was faced with a small nervous child whose eyebrow I had stitched up under an anaesthetic, and the removal of the stitches was approached with considerable caution by both of us. By using a scalpel blade No. 11 I found that I could slide the tip underneath the suture, and before any tension was felt the suture was cut.

Since then I have never used a pair of scissors to remove stitches, and no patient has ever felt one coming out.

Surgery of any kind always involves some pain to the patient, and it is our duty never to become hardened, but where possible we must use forethought to minimize pain. I should like to see scissors entirely replaced by a scalpel in the tray for removing sutures, especially in hospital, where it is so often done by dressers and junior nurses who are gaining experience.—I am, etc.,

Great Dunmow, Essex. GEOFFREY BARBER.

POINTS FROM LETTERS

Isoniazid Treatment in Advanced Pulmonary Tuberculosis

Dr. T. DONOVAN (Cork) writes: I have been using this drug since late April. The patients were inmates of St. Joseph's Sanatorium, Cork, and were mainly of the advanced incurable or acute moribund types. All the cases treated were pulmonary, 85 in number. The average age was 37. The average duration of the disease was four years. The dosage given was: First week, 100 mg. twice daily; second week, 200 mg. twice daily; third week, 300 mg. twice daily. The dose of 600 mg. per day was continued. In all cases, except six, appetite improved, weight increased, cough and sputum were diminished, temperature, when present, became normal, and there was a remarkable feeling of well-being. In eight cases cough and sputum ceased and have not recurred. In 15 cases the treatment was discontinued after two months, and, of these, eight had a recurrence of cough and sputum. There were four acute and moribund cases for whom the expectation of life was estimated to be about two months. All four revived in a most dramatic fashion and now look and feel well. One patient, aged 70, improved temporarily, then developed tuberculous toxaemia and died. Seven patients, after six weeks, developed peripheral neuritis, starting with numbness and tingling of the hands and feet, progressing, in two cases, to severe burning feelings and pain. No motor paralysis was evident. The average age of these seven cases was 45, and the average duration of illness four and a half years. Treatment was discontinued, and the dose in all other cases was reduced from 600 to 300 mg. per day. No other cases of neuritis have since occurred. After five to six days neuritis has in all cases improved; and two of the cases have resumed treatment without, so far (three weeks), recurrence of neuritic symptoms. All those who discontinued treatment and who had recurrence of symptoms have recommenced, and improvement is evident in most cases. It was noticed that patients improved more rapidly and intensely at the 600 mg. per day level.

Flying Squad Unit for Abortions

Dr. MARY A. FOLEY (London, N.W.6) writes: I would like to see a mobile ambulance unit which would take blood, sterile instruments, and anaesthesia to the home of the patient who is aborting. The general practitioner would then be relieved of the difficulty encountered in trying to get such a patient accepted by a hospital and the valuable beds could be used for waiting-list cases. Of course there are a few cases of abortion which will require hospitalization, but they are very few. I am ignorant of the economics involved, but surely the money saved from the beds would pay for the service. I suggest that the unit should be run on the same lines as a maternity hospital flying squad which could give the patient at home the treatment which she would receive in hospital. The patient needs very little nursing care after a dilatation and curettage and in the majority of cases would be much happier at home. I would be most interested to read the comments of yourself and your readers.

Dupuytren's Contracture

Dr. ERICH GEIRINGER (Edinburgh) writes: That a hereditary disposition plays a part in the aetiology of Dupuytren's contracture is by now well established. The following case concerns female twins, aged 28 years. One of them developed about two years ago a linear thickening and contracture of the palmar aponeurosis opposite the base of the right ring finger. The overlying skin is involved in the characteristic puckered fashion, but there is as yet little interference with the mobility of the finger. She is right-handed. Her left-handed sister has now developed a coarse, nodular thickening of the palmar fascia of the left hand in exactly the same anatomical position. Examination for other mirror phenomena was not possible. In neither case is there a history of prolonged or excessive pressure on the palms. Twinship, mirror phenomenon, early onset, and female sex must be an extremely unusual combination in this disorder.

Obituary

Captain ANTHONY ARTHUR HOBBS, R.A.M.C., who died at Benghazi, Cyrenaica, on October 8 of poliomyelitis, was born on January 1, 1926, and qualified M.R.C.S., L.R.C.P. in 1948. After qualification he became house-physician and anaesthetist at the Princess Alice Memorial Hospital, Eastbourne, and later worked at the Halifax General Hospital from June, 1949, until December, 1950. In the following year he entered the R.A.M.C. as a lieutenant, becoming captain a year later, and was stationed at Benghazi at the time of his death. During his stay at Halifax he married Miss Jean Astin, a member of the staff of the General Hospital, and endeared himself to all his colleagues and a large circle of acquaintances by his charming personality and his joy of life, combined with a brilliant aptitude for his work as an anaesthetist. There was no doubt in the minds of his colleagues that his ability as an anaesthetist was outstanding, and everything pointed to his rapid advancement in the specialty. His loss is irreparable, and the shock of his death is still so acute that many of us cannot realize that he is indeed dead. Our sympathy goes out to his young wife and baby.—H. I. D.

South Wales members of the British Medical Association, especially the senior generation, will have heard with regret of the death in London on October 14, at the age of 86, of Dr. J. M. MORRIS, who was in his day a tower of strength to his professional brethren. John Mudie Morris was born at Edinburgh in 1866. After taking an arts degree in classics and philosophy at the University of Edinburgh he turned to the study of medicine and graduated M.B., C.M. in 1893. After some years in general practice, mainly in South Wales, he took the Cambridge D.P.H. in 1906, and thereafter public health became his life-work. He was a pioneer in infant-welfare work, and in 1920 he became full-time medical officer of health of Neath. By his very keenness and his forward vision he found himself frequently opposed by those in authority less advanced than himself, but he was a "bonny fechter" and a true progressive. In the war of 1914–18 he served as a captain in the R.A.M.C. and was in charge of the military hospital at Neath. On his retirement from his appointment as medical officer of health in 1940 his indefatigable temperament would not permit his being put on the shelf, and he became resident medical officer at Hensol Castle, an institution for mental defectives at Pontyclun, Glamorganshire. At the end of the war in 1945 he was freed from official duties, and, with his wife, he retired to London to be with his daughter, a distinguished graduate in science of Cambridge. He was justly proud of her achievements and those of his two sons, one of whom is Professor W. I. C. Morris, professor of obstetrics and gynaecology in the University of Manchester, and the other Dr. Keith M. Morris, of Hairmyres Hospital, East Kilbride. All through his professional life Morris was an active and enthusiastic member of the B.M.A., and his tall gaunt figure was always looked for in professional gatherings. He served as joint honorary secretary of the Swansea Division from 1914 to 1923, and was president of the South Wales and Monmouthshire Branch in 1928–9. A faithful alumnus of his old university, he was a founder member of the South Wales and Monmouthshire Branch of the Edinburgh Graduates Association, and, true to the land of his birth, he was foremost in the activities of the Swansea and South Wales Caledonian Society, of which he was also a founder.

We are indebted to Dr. H. R. FREDERICK for the following appreciation: Morris's loyalty to the Association and the profession was well known. Uncompromising in his stand for what he believed to be right, he was often thought to be obstinate and difficult, but in reality he was a man who loved his fellow men, and with his keen sense of humour enjoyed twitting them for their shortcomings. Correspondence with Morris, mainly on postcards, and written in an angular script, was a joy, and when deciphered revealed an unusual twist of language. A Scot of Scots, he was always a student, and even in retirement he was an enthusiastic participant in Workers' Educational Association classes in English literature and philosophy.

In view of the Annual Meeting of the B.M.A. to be held at Cardiff next year it may be worth recalling that it was at Swansea in 1903 that the new constitution of the Association was introduced and where the first Annual Representative Meeting was held. There cannot, now, be many survivors of the first Representative Body besides the perennial Alfred Cox, but Morris recalled with interest his attendance at that meeting, although he was not present in any official capacity. In those years, in the early part of the century, local medical societies were active, and Morris was prominent in the affairs of the Swansea Society. His views were sometimes not those of the majority, but he retained the respect and admiration of those associated with him, both publicly and privately. In him I have lost a valued friend, and the profession one who served it faithfully and with devotion and integrity. Our sympathy goes out to Mrs. Morris, herself a native of Neath, and to her sons and daughter in their loss.

Dr. WILLIAM PEACH HAY, who died at Peterborough on October 17 in his 83rd year, was the son of the editor of the *Arbroath Guide*. He studied medicine at the University of Edinburgh, where he graduated M.B., C.M. in 1891. During his final year as a medical student he went on a whaling expedition in the Arctic, and after graduating he entered the Colonial Medical Service, being appointed assistant surgeon at Lagos. His period in the Service completed, he then acted as an assistant in a Yorkshire mining practice for a short time until, in 1897, he settled at Peterborough, where he continued in active practice for the very long period of 54 years, until ill-health compelled his retirement last year. He lived to see an isolated railway community develop into a prosperous city. Dr. Peach Hay was a man of wide interests. Besides being a member of the board of management of the local hospital he was the first and only chairman of the Soke of Peterborough panel committee, throughout the life of which he represented the area at the annual Panel Conference. He was a keen supporter of the British Medical Association, being elected chairman of the Peterborough Division in 1936–7. Not only was he a founder 25 years ago, but he remained until his death as the only president of a very active local Caledonian Society. A deep scientific interest led him to membership of the Royal Physical Society of Edinburgh. Dr. Peach Hay was a true family doctor and was as welcome in the cottage as in the "big house." He loved his fellow man and he was the most lively and entertaining host. Kind and considerate to his colleagues, he was ever ready with friendly and sound advice. His recreations were varied and ranged from a true love of the theatre to the metal-worker's bench. He leaves a widow, one son, and two daughters, to whom we extend our sympathy in their loss.—J. I. W.

We record with regret the death of Dr. EDMUND KEAN at Dover on October 24 at the age of 60. Edmund Kean was born on August 1, 1892, the eldest son of the late Dr. Thomas Kean, of the Aran Islands, off the coast of Galway. He studied medicine at the National University of Ireland, where he graduated M.B., B.Ch. in 1916, and he took the D.P.H. in 1931. In the war of 1914–18 Dr. Kean served in the R.A.M.C., and after the cessation of hostilities he transferred to the Indian Medical Service, later becoming senior medical officer at Bushire, in Persia. Altogether he served some 20 years in India and the Middle East. On his return to this country in 1932 he became deputy medical officer to the Port of London Authority, and three years later he was appointed port medical officer at Dover. In the last war he served in the R.A.M.C. from 1939 to 1943, when he was obliged to relinquish his commission on

account of ill-health. In 1950 he was appointed a medical inspector of aliens. A sound naturalist, Dr. Kean compiled a rat and flea index of the Port of London, a work which at the time was considered to be of importance, but being of a modest and retiring nature he asked that his name should not be published in connexion with it.

Dr. ALEXANDER MAITLAND EASTERBROOK, a well-known and highly respected Midlothian practitioner, who died at Eskbank, Dalkeith, on October 25, aged 83, was born at Dalkeith on November 1, 1868, and was educated at George Watson's College, Edinburgh, and at Dulwich College, where he was captain of the rugby second XV. After a distinguished career at the University of Edinburgh, where he won a Grierson bursary in chemistry, botany, and zoology and the James Scott scholarship in midwifery and gynaecology, he graduated M.B., C.M., with first-class honours, in 1893. He then became house-physician to the late Sir Thomas Grainger Stewart at Edinburgh Royal Infirmary, and this appointment was followed by a resident post at the Edinburgh Royal Maternity and Simpson Memorial Hospital. With such a record there was more than one path in the field of medicine he might have followed, but he chose general practice and entered into partnership with, and later succeeded, the late Dr. William Spalding at Gorebridge, Midlothian, the centre of an extensive country and mining district. For about 44 years he worked in this area, gaining the respect and affection of his patients, who subscribed towards a public presentation when he retired from practice in 1937. He took a prominent part in local affairs, and after the 1914–18 war it was chiefly under his guidance that the money locally subscribed for a war memorial was utilized to found the Gorebridge District Nursing Association. Dr. Easterbrook took a deep interest in the work of the British Medical Association, acting as honorary secretary of the Lothians Division from 1911 to 1917 and as chairman of the Division from 1909 to 1911 and in 1937–8. He was also president of the Edinburgh Branch from 1932 to 1934. During the prolonged discussions with the Government over the conditions of work and payment under the National Insurance Act of 1911, and when every effort was being made to increase the membership of the Association, he worked untiringly, and was mainly responsible for bringing the membership in Midlothian up to full strength. For several years he was the representative of the Lothians Division at the Annual Meetings of the Association, and he went to Melbourne when the B.M.A. held its Annual Meeting there in 1935. He was a member of the Midlothian panel committee from the date of its inception till he retired. Another important body on which he served was the Scottish Colliery and Public Works Surgeons' Committee, which was composed chiefly of delegates from every colliery area in Scotland. Before the formation of this committee the contract rates of payment for medical attendance on the workers' dependants were arranged locally by districts and varied in different areas: after the committee's establishment a flat rate of payment at all collieries was introduced, an arrangement which proved highly satisfactory to doctors and workmen alike. The committee, which did excellent work, was automatically dissolved in 1948 on the introduction of the National Health Service. Dr. Easterbrook was one of a family of brothers all of whom made their mark in life, perhaps the most distinguished being the late Dr. C. C. Easterbrook, who was physician-superintendent of the Crichton Royal Institution from 1908 to 1937. He died in 1949. Dr. and Mrs. A. M. Easterbrook celebrated their golden wedding in 1950. He is survived by his widow, two sons, and two daughters, one of whom is a doctor.—J. McK.

The recent death of Dr. H. F. NORTHEY in London after an operation has robbed Northern Ireland of one of its outstanding medical practitioners. Hector Francis Northey was born at Belfast on January 2, 1905, and was educated at the Royal Belfast Academical Institution and at Queen's University, Belfast. After graduating M.B., B.Ch. in 1930 he was appointed resident medical officer to the Belfast Infirmary, and then he settled at Helen's Bay, County Down, where he conducted an extensive practice throughout the north of County Down, being loved by all his patients for his skill, his kindness, and his gentle manner. His appointment as a J.P. to the local bench was a mark of the regard in which he was held by the community. He took the D.P.H. in 1939, and during the war he was medical officer to a coastal battery and a prisoner-of-war camp. He was also medical officer to the County Down Branch of the British Red Cross Society. A keen sportsman, he took a great interest in yachting, golf, and rugby football. He was honorary secretary of the Royal Ulster Yacht Club, a member of the Royal North of Ireland Yacht Club, and of the Royal Belfast and Helen's Bay golf clubs. His failing health in recent years must have been a sore trial to him, and only his devoted wife knew how great an effort he had to make in order to continue his work. The deep sympathy of his fellow practitioners, who have lost a trusted and a helpful colleague, goes out to her at this time.—H. H. C.

Medical Notes in Parliament

Accommodation for Mental Defectives

Mr. BERNARD BRAINE on November 5 drew attention to the shortage of accommodation for mental defectives. Institutions in England and Wales accommodated some 49,000 defectives, while of the 8,000 awaiting admission half were children. Many children remained on the waiting-list for years. The earlier the training of high-grade defectives began the quicker and better the results, but too often children were not admitted until it was too late for anything to be done for them. The problem of accommodation was growing. One institution in Essex should house 1,443 patients; it had nearly 1,700 and a waiting-list of 543, most of whom were children. The numbers on this waiting-list had grown fivefold since the appointed day. Earlier ascertainment of a mentally defective condition was the main contributory cause to the growth of the problem. Three things were mainly required. The first was increased accommodation, the second more staff, and the third more voluntary workers to care for defectives outside the institutions. Insufficient elasticity was allowed to hospital management committees in the appointment and pay of their staff. It was wrong that a sister at a general hospital who was anxious to do mental deficiency nursing could receive only the pay of a probationer nurse if she transferred.

After Mrs. BRADDOCK had described the position in Liverpool, where there were 104 cases on the waiting-list, many having been there a long time, Miss HORNSBY-SMITH replied to the debate. She said the shortage of accommodation was serious, but 3,066 new beds in regional hospital board hospitals had been opened for mentally defective patients since the appointed day. In addition many unstaffed beds had been equipped, but the waiting-list had risen from 3,939 on the appointed day to 7,929 at the beginning of 1952. There were also 5,000 mentally deficient patients in mental hospitals who should be in mental-deficiency institutions, besides children in homes and orphanages who also should be in institutions. The Ministry needed 15,000 additional beds for mental defectives. In the first years of the National Health Service regional hospital boards had not all paid as much attention to this side of their medical responsibilities as to others, but the average percentage of hospital capital expenditure allocated for mental treatment and mental-deficiency treatment had risen from 19.8% of total capital expenditure in 1951 to 26.1% in 1951–2. For mental-deficiency treatment alone the proportion of capital expenditure allotted in 1950–1 was 7.1%; in 1951–2

11.4%; and in 1952–3 it would be 10.4%. In 1948 the total of full-time nurses in hospitals which were mainly for mental defectives was 5,941, and this year it was 6,542.

Limbless Ex-Servicemen

Mr. JAMES SIMMONS brought to the notice of the House on November 6 the question of allowances to the aged limbless. He said that in the first world war 45,500 suffered amputation of one or more limbs. Of these men 24,500 survived. They were dying off at the rate of 1,000 a year. With increasing age the burden of wearing an artificial limb increased. The limbless alone among war-disabled were tied to a fixed table of assessments. No regard was paid to the worsening of their condition. He asked whether the terms of reference of the Rock Carling Committee could be extended to inquire into the long-term effect on the general health of the limbless and the effect in the case of single amputations on the remaining leg.

Mr. HEATHCOTE AMORY, Minister of Pensions, said that as a result of the Hancock Committee the 24,500 limbless of the 1914–18 war did in fact have their assessments raised. He could not help feeling that there was some substance in the argument that the difference between a fit man and a disabled man was wider in the case of elderly people. The question was how much difference there was and if it was enough to justify special compensation. He could not discriminate in favour of one category unless he had medical evidence on which he could act. At present no such medical evidence was available. The Hancock Committee had concluded that it was impossible to establish that the functional effect of an injury depended so directly on the injured person's age as to render it practicable to fix different assessments for different age groups. He hoped that the Rock Carling Committee would report to him within two months. The present policy of the Ministry was to deal with each individual case on its merits. Where there was anything like sepsis or stump trouble, or any other complicating factor, the case was reviewed and an increase given if justified.

Medico-Legal

HYPERSENSITIVITY TO AMETHOCAINE

[FROM OUR MEDICO-LEGAL CORRESPONDENT]

An unusual case of death due to hypersensitivity to amethocaine was the subject of an inquest on October 9, 1951, before the Deputy Coroner for Hertfordshire. The drug was used as a local analgesic for bronchography.

A man aged 49 was admitted to hospital on September 18 suffering from pneumonia. He made a good recovery, and was to have been discharged on October 6. But he had suffered intermittently from chest trouble since the age of 21 and had had pneumonia on six previous occasions, some within the last two years, and he was therefore advised to have an *x*-ray bronchogram taken before leaving hospital.

He agreed to this course, and arrangements were made for it to be done on October 4. He had been examined by a specialist and passed fit for radiography. On October 3 his sensitivity to cocaine was tested by a routine method and was normal. At 3 p.m. on October 4 the medical registrar started to spray his throat with a 5% solution of amethocaine. By 3.8 p.m., when a little more than 3.5 ml. of the solution had been sprayed into the patient's throat, the doctor considered the man had had enough. During the spraying he had made no complaint. At 3.10 p.m. he became restless and almost at once began to go into convulsions. Oxygen was ordered, but he became cyanosed; twitching was followed by full convulsions, and he lost consciousness. Respiration quickly ceased, and in spite of treatment he died at 3.30 p.m.

At necropsy gross oedema of the glottis and some oedema of the larynx were found. The larynx, trachea, and bronchi contained much thick mucus and watery fluid, and there were many petechial haemorrhages in the trachea. The left lung was small and congested, with basal bronchiectasis and bronchi containing clear mucus. The right lung was large and emphysematous, with a slight mediastinal shift to the left. There had been an almost complete stoppage of the air passage.

The cause of death was acute oedema of the glottis and inhalation of mucus. Such a reaction to a 5% amethocaine solution was stated to be a most unusual occurrence, depending not on the amount of the dose but on hypersensitivity of the patient. A verdict of death by misadventure was recorded.

The Services

A *Supplement* to the *London Gazette* has announced the following appointments and mentions in dispatches in recognition of gallant and distinguished services in Malaya during the period from January 1 to June 30, 1952:

C.B.E. (Military Division).—Colonel (Temporary) N. P. Breden, R.A.M.C.

M.B.E. (Military Division).—Majors (Temporary) A. P. Dignan, and F. J. Humble, R.A.M.C.

Mentioned in Dispatches.—Colonel W. A. D. Drummond, C.B.E., late R.A.M.C.; Lieutenant-Colonel (Temporary) H. R. Hartnell, M.B.E., and Captains E. L. Copley, I. W. Griffith, and C. J. H. Mann, R.A.M.C.

A *Supplement* to the *London Gazette* has announced the following awards:

First, Second, and Third Clasps to the Territorial Efficiency Decoration.—Colonel (Honorary Brigadier) G. J. V. Crosby, C.B.E., T.D., Q.H.P., R.A.M.C. (Honorary Colonel of a T.A. Unit).

First and Second Clasps to the Territorial Efficiency Decoration.—Colonel W. H. D. Patterson, T.D., and Major G. A. W. Neill, T.D., R.A.M.C.

Territorial Efficiency Decoration and First and Second Clasps.—Major F. W. Widgery, R.A.M.C., retired.

Territorial Efficiency Decoration.—Major (Honorary Lieutenant-Colonel) W. L. Brown, D.S.O., Major F. J. W. Hooper, R.A.M.C.; Honorary Major C. St. Johnston, R.A.M.C., retired.

Universities and Colleges

UNIVERSITY OF OXFORD

In Congregation on November 1 the degree of D.M. was conferred on J. Badenoch and A. I. Spriggs.

The Theodore Williams Scholarship in Physiology for 1952 has been awarded to Antony Babington Herring (Brasenose College).

UNIVERSITY OF CAMBRIDGE

The Council of the Senate of the University has gratefully accepted the offer of the Nuffield Foundation of a grant of £4,700 a year for three years for work on cellular biology to be conducted under the direction of Professor David Keilin in the Molteno Institute of Biology and Parasitology.

Professor H. R. Dean, Master of Trinity Hall and Professor of Pathology, has been re-elected to the General Medical Council as representative of the University, for five years from October 22, 1952.

Professor A. D. Gardner, Regius Professor of Medicine in the University of Oxford, has been appointed Rede Lecturer for 1953.

Roche Products Ltd. have made a grant of £500 a year for three years towards the cost of research on chemical radio-sensitizers in the Department of Radiotherapeutics under the direction of Professor J. S. Mitchell, F.R.S.

In Congregation on October 11 the following degrees were conferred:

M.B., B.CHIR.—*J. D. H. Slater, *D. N. H. Owen, *L. B. P. Hartley, *M. A. Baddoo, R. J. H. Harris, J. H. Kerr, P. G. Allen.

In Congregation on October 25 the following degrees were conferred:

M.D.—M. O. J. Gibson, I. C. K. Mackenzie, R. G. Law, Portia G. Holman.

M.B., B.CHIR.—J. D. Richardson and A. Fairley (by proxy).

*By proxy.

UNIVERSITY OF ST. ANDREWS

At a graduation ceremonial held on October 10 the degree of M.D. (with honours) was conferred upon J. W. Smith, M.B., Ch.B.

UNIVERSITY OF DUBLIN

SCHOOL OF PHYSIC, TRINITY COLLEGE

J. K. Craig has been approved at the examination for the degree of M.D.

UNIVERSITY OF LONDON

The following candidates have been approved at the examinations indicated:

ACADEMIC POSTGRADUATE DIPLOMA IN CLINICAL PATHOLOGY.—M. Akram, J. A. Campbell, Jean E. Duncan-Taylor, M. M. Friedman, C. E. Marshall, G. A. K. Missen, Doris C. Peiris, W. D. N. Watson, K. H. White, Mary I. Wright, S. S. H. Zaidi.

EXTERNAL DIPLOMA IN CLINICAL PATHOLOGY.—G. Aung, R. McP. Cross, D. Hewspear, J. Ward.

The following candidates at the London School of Hygiene and Tropical Medicine have been approved at the examination indicated:

ACADEMIC POSTGRADUATE DIPLOMA IN PUBLIC HEALTH.—V. Poonoosamy, W. D. Ratnavale.

UNIVERSITY OF WALES

THE WELSH NATIONAL SCHOOL OF MEDICINE

The following candidates have been approved at the examination indicated:

M.B., B.CH.—*Hygiene:* W. H. Allen, Jane I. K. Binnie, W. G. Brown, D. L. Crosby, Marian H. Dadaczynski, *A. B. David, D. R. Davies, S. L. Davies, *Joan M. Evans, L. T. I. Evans, H. J. Grosz, Margaret J. Hicks, R. M. Hodges, J. H. Hughes, *J. A. Hutchison, G. A. S. Ireland, D. T. James, D. S. Jones, J. T. Jones, W. P. T. Kime, S. Koziell, W. J. Manson, E. H. Massey, *Valerie Matthews, D. C. Morgan, J. G. Morgan, J. E. Morris, R. A. Owen, G. O. Parry, E. E. Payne, H. A. Rees, J. Rees, I. D. G. Richards, J. M. Richards, A. G. Roberts, Denise Y. Sheppard, A. D. M. Smith, J. W. G. Smith, W. G. C. Strawbridge, J. R. Tighe, D. B. M. Williams, C. G. Young.

The following candidates at the Welsh National School of Medicine have satisfied the examiners at the examination indicated:

TUBERCULOUS DISEASES DIPLOMA.—A. Kabin, R. T. Kakade, E. Robinson.

*With distinction.

UNIVERSITY OF LIVERPOOL

The following candidates have been approved at the examination indicated:

FINAL M.B., CH.B.—*Part I:* W. A. Downie, Florence M. Duckenfield, M. W. Fowles, H. G. Harding, T. R. T. Hughes, J. L. Mason, Anne D. Micah, J. M. Nichols, W. V. N. Pugh, A. Roberts, R. H. Thomas, T. Trace, G. H. Worsley.

FINAL M.B., CH.B.—*Part II:* J. R. Akers, T. R. W. Cowell, Diana M. F. Daniel, M. A. R. Eslick, D. N. Guest, C. D. James, J. C. Jacques, G. M. Mason, M. Pearson, D. F. Rice, G. S. Roberts, A. M. Stewart, Gwladys E. P. Williams, P. J. J. Wren.

UNIVERSITY OF LEEDS

The title of Emeritus Professor has been conferred on James Walter McLeod, M.B., Ch.B., F.R.S., on his retirement from the Brotherton Chair of Bacteriology.

Alan Victor Pollock, M.B., Ch.B., F.R.C.S., has been appointed Senior Registrar and Tutor in Surgery, from November 1.

Percival John Moir, F.R.C.S., who held the Chair of Surgery in the University from 1940 to 1946, and who has been elected Dean of the Faculty of Medicine, has been appointed Professor of Surgery from October 1. For the time being Professor Digby Chamberlain will continue to act as head of the Department of Surgery.

UNIVERSITY OF SHEFFIELD

The following full-time appointments are announced: *Lecturer in Therapeutics*, S. Oleesky, M.D., M.R.C.P. *Temporary Lecturer in Therapeutics*, R. S. Weetch, M.B., M.R.C.P. *Temporary Lecturer in Child Health*, D. M. G. Beasley, M.B., M.R.A.C.P.

E. K. Blackburn, M.D., F.R.F.P.S., D.R.C.O.G., has been appointed part-time Honorary Lecturer in Pathology.

Dr. Sheila M. Stewart has resigned the position of Honorary Demonstrator in Bacteriology on taking up a Research Fellowship in the University of Edinburgh.

ROYAL COLLEGE OF PHYSICIANS OF LONDON

At a quarterly comitia of the College held on October 30, with the President, Sir Russell Brain, in the chair, Dr. Geoffrey Bourne, Professor E. C. Dodds, F.R.S., Professor Robert Platt, and Dr. J. T. Ingram were elected Councillors of the College; Dr. A. Feiling was elected representative on the committee of management; Sir Russell Brain, Sir Harold Boldero, Dr. W. G. Barnard, Dr. A. M. Cooke, and Sir Allen Daley were re-elected members of the standing joint committee of the three Royal Colleges; Dr. C. E. Newman was appointed representative on the examination and tuition advisory board of the Association of Medical Records Officers; and Dr. S. W. Davidson was appointed representative on the Council of King's College, Newcastle, in the University of Durham.

The following candidates, having satisfied the Censor's Board, were elected Members of the College: J. A. Balint, M.B., C Berman, M.D., S. O. Boldy, M.D., T. H. Bothwell, M.B., P. D. Bryant, M.D., A. R. Buckley, M.B., E. J. M. Campbell, M.D., T. B. Cullity, M.B., R. A. Dale, M.B., H. E. F. Davies, M.D., W. E. B. Edge, M.B., A. W. H. Evans, M.B., B. J. S. Harley, M.D., G. Hildick-Smith, M.B., B. I. Hirschowitz, M.B., D. G. Julian, M.B., L. H. Klugman, M.B., C. D. Lacey, M.B., W. L. B. Leese, B.M., M. A. Macan-Markar, M.D., Lisa E. Mandelbaum, M.B., J. S. Moos, M.D., L. McA. Reid, M.B., H. R. C. Riches, M.B., S. J. G. Semple, M.B., N. K. Shinton, M.B., P. V. Thacker, M.B., A. B. Tompkins, M.B., S. M. Vine, M.B., G. Walker, M.B., P. R. Walsh, L.R.C.P., G. Walters, M.B., D. G. C. Whyte, M.D., Major, R.A.M.C., G. M. Woodwark, M.B., C. R. Woolf, M.D.

Licences to practise were conferred upon the following 123 candidates (including 28 women) who had passed the final examination in Medicine, Surgery, and Midwifery of the Conjoint Board and who have complied with the by-laws of the College: C. W. M. Adams, H. R. Alpin, Ursula M. Anderson, J. L. Andrews, J. A. R. Anson, D. T. C. Barber, D. W. Barnes, I. R. Beale, J. K. H. Benson, S. W. Bissell, S. Bourne, A. J. Bowdler, J. A. D. Briggs, J. J. Brown, J. R. G. Brown, H. P. Charles, R. D. Choudhury, C. S. M. Chown, Evelyn Coates, J. H. Corbett, B. J. Cremin, L. M. Davis, J. C. Denmark, L. Essex, Anne C. Evans, M. D. C. Evans, J. Fairley, Patricia M. Firkins, Margaret Fisher, W. A. Forrest, J. M. Foster, A. I. Fram, Hannah French, Anna L. Frenkiel, G. R. K. Frost, R. E. Fryer, H. G. Gage, R. A. Gawn, H. M. Georgeson, R. B. Glover, G. R. Grant, D. J. Green, J. M. S. Grieve, Elizabeth A. Grimditch, E. H. L. Harries, Joyce Harrison, M. N. Harrison, D. Harvey, A. Haylock, Natalie J. Holloway, H. A. Hosking, N. Howard, C. K. Hudson, Kathleen M. Huntington, C. F. Hutchison, I. B. Johnson, H. S. Jones, H. D. Jones, T. P. Jupp, Patricia M. Kenney, J. B. Kenyon, D. W. King, J. R. Kirkup, W. R. Kynan, S. R. S. Laing, Lesley P. Leader, Rachel E. Lee, Monica C. Lewin, R. J. Lewis, H. E. Lichtenstein, W. J. McCall, Kathleen M. McCartie, T. McCormick, I. R. McDonald, J. U. MacWilliam, W. B. Manley, R. A. Matthews, P. D. Meers, D. C. Morrell, T. F. Morris, R. J. Murray, M. R. Newell, A. S. Nicholas, F. I. Partington, Naomi I. Penfold, D. E. Phillips, Grace D. Pinkerton, A. J. Platts, J. F. W. Rail, J. E. Rees, H. F. Reichenfeld, J. W. Rentoul, C. E. Rhodes, W. A. G. Roper, A. D. Rowlands, J. F. Ryan, Mary S. Shenai, Eva H. Short, Anne M. Shuffrey, Elizabeth L. Siddle, I. F. Smith, D. N. Stathers, Kathleen M. Stevenson, J. W. Strain, J. F. Sturridge, J. H. Swallow, E. McK. Sycamore, Eva S. Szmulewicz, Audrey M. Tabor, B. D. Thomas, Constance P. F. Thomas, Heather B. Thompson, Lorna G. Tolchard, B. L. M. Turner, J. R. Turner, N. D. Walsh, D. Watkins, J. H. White, R. Wilton, R. P. Wise, A. R. Worters, D. A. Wright, J. D. Wright.

Diplomas were granted jointly with the Royal College of Surgeons of England, as follows:

DIPLOMA IN MEDICAL RADIODIAGNOSIS.—W. A. Copland, R. S. Crone, E. O. Field, J. V. Goodman, R. G. Grainger, Dinah C. M.

Henderson, M. Hurwitz, S. P. Kumar, J. W. Laws, J. C. Linn, G. N. Mukherjee, R. W. Wilkinson, S. F. Wyner.

DIPLOMA IN MEDICAL RADIOTHERAPY.—Daphne S. A. Anderson, P. B. Kunkler, G. D. Smith.

Diplomas in Tropical Medicine and Hygiene, in Child Health, in Physical Medicine, and in Industrial Health were granted, jointly with the Royal College of Surgeons of England, to the candidates whose names appear in the report of the meeting of the Royal College of Surgeons of England printed below.

ROYAL COLLEGE OF SURGEONS OF ENGLAND

At a meeting of the Council of the College held on October 9, with Sir Cecil Wakeley, President, in the chair, Sir Charles Symonds and Professor Harold Dew, of Sydney, were appointed the Sir Arthur Sims Commonwealth Travelling Professors for 1953.

The first James Berry Prize was awarded to Mr. R. H. C. Robins for his essay on "The Treatment and Preservation of the Injured Hand."

Dr. B. D. Wyke was appointed senior lecturer in the department of physiology.

A Leverhulme Research Scholarship was awarded to Mr. A. E. Kark, of the Witwatersrand University.

Mr. Brian Greenwood (St. Thomas's Hospital, late of Heath Grammar School, Halifax) was admitted as a Macloghlin scholar.

A diploma of Fellowship of the College was granted to G. S. Pestell (Melbourne) and a diploma of Membership to J. H. Swallow (London).

Diplomas in Tropical Medicine and Hygiene, in Child Health, in Physical Medicine, and in Industrial Health were granted, jointly with the Royal College of Physicians of London, as follows:

DIPLOMA IN TROPICAL MEDICINE AND HYGIENE.—S. K. Ally, G. Belios, K. H. Blaauw, J. Bonne, Matilda J. Clerk, D. F. Clyde, K. R. J. Coates, K. J. Covell, J. C. Crook, J. S. Davis, S. C. Desai, S. S. Epstein, H. Foster, D. G. Garrow, A. Gerada, S. R. S. Godkin, E. G. Hardy, J. R. Harries, Monica M. Hogben, B. O. Igwebe, Gillian F. Jacob, P. A. H. Jenniskens, Elizabeth E. Johnson, P. K. Jungawalla, T. Karadshy, M. Khalaf, M. N. Khan, A. R. Mubarak, N. Panikbutra, U. K. Perera, B. Prasad, S. K. Roy, F. Saliba, W. B. Seale, D. H. Shennan, S. Singh, A. W. Stinton, D. A. T. Tizard, R. A. R. Topping, P. Tuchinda, C. J. Xuereb.

DIPLOMA IN CHILD HEALTH.—L. McC. Armstrong, H. Buckstein, J. F. J. Collins, June P. Cooper, Winifred Danaraj, B. M. Davies, Pamela Deas, G. L. de Silva, J. A. C. de Silva, N. Feldman, Nellie P. Fernando, P. T. A. P. Fernando, Joan Ford, Yvette A. P. Franklin, O. P. Gray, Ruth F. Harris, W. L. F. Hatchuel, Frances M. Hill, Mary A. le C. Hills, C. Hooja, Pamela J. Houchin, W. W. Jones, Margaret Kennedy, Barbara Kilpatrick, C. W. Lankester, I. C. Lewis, T. K. Lim, S. Loganadan, S. K. Majumdar, Patricia A. Monk, E. A. Nieman, Olwyn K. Ockelford, D. J. A. L. Panditharatne, Dina Patuck, G. J. V. Perera, P. L. Pickering, Barbara M. Philpott, Quah Quee Guan, T. A. I. Rees, Frances L. J. Robinson, Pauline M. Seymour-Cole, Katherine A. H. Smith, C. Srinavasan, June Stephenson, Gwendolyn R. Tapp, F. Taylor, N. Van der Merwe.

DIPLOMA IN PHYSICAL MEDICINE.—P. J. R. Nichols, J. G. Parish, R. C. Robb.

DIPLOMA IN INDUSTRIAL HEALTH.—K. M. Basu, A. T. Halliday.

Hospitals were recognized under paragraph 23 of the F.R.C.S. regulations as follows: Victoria Hospital, Accrington, *additional recognition*, house-surgeon for six months; *redesignation of post already recognized*, surgical registrar (formerly senior house-surgeon). Altrincham General Hospital, *additional recognition*, surgical registrar; senior house officer (surgical); junior house officer (surgical), all for six months. St. Martin's Hospital, Bath, two house-surgeons (general) for six months. Black Notley Hospital, Braintree, *confirmation of temporary recognition*, general surgical registrar, orthopaedic registrar; general house-surgeon (until October 31, 1953); orthopaedic house-surgeon, all for six months. Bolton Royal Infirmary, *additional recognition*, senior house officer (general surgery); senior house officer (orthopaedic); senior house officer (casualty), all for six months; *redesignation, surgical registrar* (formerly resident surgical officer); senior house officer (formerly assistant resident surgical officer). Bolton District General Hospital, surgical registrar; senior house officer in surgery, both for six months. Chester Royal Infirmary, *paragraph 23b*, registrar (ophthalmic), for one year. Princess Alice Memorial Hospital, Eastbourne, house-surgeon (general surgery); house-surgeon (orthopaedic surgery), each for six months. St. Mary's Hospital, Eastbourne, first and second house-surgeon, each for six months. Princess Elizabeth Orthopaedic Hospital, Exeter, registrar, three senior house officers, all for six months. West Norfolk and King's Lynn General Hospital, *additional recognition*, two house-surgeons, each for six months. Lambeth Hospital, *paragraph 23b*, ophthalmological house-surgeon for six months. St. Charles' Hospital, London, *decennial revision*, two registrars for six months. St. Mary Abbots Hospital, London, *decennial revision*, registrar for one year; two house-surgeons for six months. St. Stephen's Hospital, London, *additional recognition*, house-surgeon (general) for six months. North Riding Infirmary, Middlesbrough, *paragraph 23c*, registrar (ear, nose, and throat); house-surgeon (ear, nose, and throat). City General Hospital, Sheffield, *revision of recognition, general surgery*, registrar for one year; senior house officer for six months; two house-surgeons for six months; *casualty surgery*, two casualty officers for six months (as from 1954); *orthopaedics*, registrar for six months; *thoracic surgery*, registrar and senior house officer, both for six months. Warwick Hospital, surgical registrar (general surgery); orthopaedic registrar; senior house officer to general surgical and orthopaedic units, all for six months. Wolverhampton and Midland Counties Eye Infirmary, *paragraph 23b*, senior house officer for one year; two house officers for six months.

ROYAL COLLEGE OF PHYSICIANS OF EDINBURGH

At a quarterly meeting of the College held on November 4, with the President, Dr. W. A. Alexander, in the chair, the following were elected Fellows of the College: T. F. Corkhill, J. Lawson, J. Kinnear, J. M. Alston, A. W. E. Soysa, F. Himmelweit, T. Scott, J. J. J. Giraldi, D. R. MacCalman, R. W. D. Turner, W. I. Card.

The following were elected Members of the College: A. D. T. Govan, G. W. A. Dick, J. C. Bowe, K. B. Kapur, J. Harper, D. C. Campbell, J. S. Sodhy, T. F. McCarthy, M. A. Khan, Sheenah J. M. Russell, M. G. E. Hanno, H. Sadik, B. R. Hillis, A. F. Fahmy, B. L. Agarwal, E. J. D. Nariman, R. M. Kapadia, O. T. Khoo, W. J. Mitus, L. Mirabel, Mariella Fischer-Williams, I. R. Yudaken, B. A. Akhtar, B. Seltzer, S. C. Shah, S. A. Singh, H. J. H. Hiddlestone, A. D. McInnes, J. H. Greig, H. Stein, A. W. M. Smith.

ROYAL COLLEGE OF SURGEONS OF EDINBURGH

At the annual meeting of the College held on October 22 the following officers were elected for the ensuing year: *President*, Professor Walter Mercer; *Vice-president*, Mr. W. Quarry Wood; *Secretary and Treasurer*, Mr. J. J. Mason Brown; *Representative on General Medical Council*, Sir Henry Wade; *Conservator of Museum*, Mr. J. N. J. Hartley; *Convenor of Museum Committee*, Mr. John Bruce; *Librarian*, Dr. Douglas Guthrie.

The following candidates, having passed the requisite examinations, were admitted Fellows: A. A. Alidina, G. S. Babbar, K. L. Barnes, A. K. Brown, J. V. Desai, S. S. Khoury, M. Khudabux, H. Kramer, R. C. W. Lowe, J. D. Malloch, N. Noble, R. D. Oatway, F. F. Sandor, L. A. Scrivin, G. S. Sekhon, S. K. Sinha, J. R. Smith, D. M. Stevens, N. P. Stracey, S. E. Wijetilaka.

ROYAL FACULTY OF PHYSICIANS AND SURGEONS OF GLASGOW

At the annual meeting of the Royal Faculty of Physicians and Surgeons of Glasgow held on November 3 the following officers were elected for the ensuing year: *President*, Mr. Andrew Allison; *Visitor*, Dr. Stanley G. Graham; *Honorary Treasurer*, Mr. Matthew White; *Honorary Librarian*, Dr. Archibald L. Goodall; *Representative on General Medical Council*, Mr. Andrew Allison.

ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS

At a meeting of the Council of the College, held on September 26, with the President, Dame Hilda Lloyd, in the chair, the following were admitted to the Membership: Lily Arratoon, J. D. Arora, J. L. M. Bean, A. C. Bhoumik, A. D. H. Browne, G. H. Burgess, G. G. Champion, S. Chinnatamby, G. R. Clare, J. F. Correy, N. K. Crooke, G. E. Cummins, A. M. Dawson, R. D. De Vere, D. T. Dodds, C. P. Douglas, R. Dowie, S. K. Dutt, J. Firth, Aileen C. Foley, M. S. Forrest, W. T. Fullerton, R. L. Gadd, D. F. P. Gordon, W. J. Gordon, J. J. Handler, A. Hunter, Daphne M. E. Kayton, R. D. Macbeth, I. A. McDonald, Margaret W. Macgregor, T. McG. McNie, T. P. Magee, A. G. Mathew, P. R. Myerscough, E. P. D. O'Neill, J. G. O'Sullivan, Marjorie M. Paterson, A. Persey, G. W. Prueter, D. Puflett, Marie Quadros, M. B. Quane, B. B. Rakshit, H. Rees, Monica M. A. Reford, C. A. Simmons, E. L. Trott, Mary E. Walker, R. A. Warren, H. B. Watson, J. A. Williams.

CONJOINT BOARD IN SCOTLAND

The following candidates, having passed the final examinations, have been granted the diploma of L.R.C.P.Ed., L.R.C.S.Ed., L.R.F.P.S.Glas.: H. E. O. Adefope, Caroline D. Bell, I. K. Bond, Mary R. Cardwell, Stella M. Conway, R. M. Gabriel, Joan Gilbert, C. P. Hargovan, E. A. Heywood, E. P. Jones, A. Y. Kpeglo, Heather J. Lopert, P. A. P. Mackenzie, R. W. Noblett, J. W. Parsons, J. Peacock, E. S. O. Pratt, W. Ritchie, Patricia J. A. Stewart, A. El-S. A. Touba, J. L. Tuton.

ROYAL AUSTRALASIAN COLLEGE OF PHYSICIANS

The following candidates, having satisfied the Board of Censors in Australia, were admitted to the Membership of the College in October: J. Beveridge, R. S. Colton, M. Faunce, Alison K. Garven, D. F. King, G. S. Nagy, A. Jean Palmer, and I. S. Wallman.

Vital Statistics

The 1951 Census

The second and final part of the 1% sample of the 1951 Census now published deals with the characteristics of the heads of private households, the composition of private households, the population enumerated in institutions, hotels, etc., education, birthplace and nationality, fertility, and Welsh and Gaelic languages for the whole of Great Britain.

The head of the household was married in 11m. of the 14½m. private households. Over 8m. of the households (57%) contained no child under 16 and in over 3m. there was only one child. Almost one household in two had one and not more than one earner, 39% had more than one earner, and 14%, mainly one- or two-person households, contained no earner at all. A little more than three-quarters of a million married couples lived in other people's homes. The majority of them were married children of the head of the household, but in 5% of the cases they were parents of the head. In addition there were nearly half a million widowed or divorced persons living with their married children. There were only 178,000 resident domestic servants in private households in 1951 compared with 706,800 in 1931. 96% of the population was born in Great Britain in 1951 compared with 97% in 1931. Nearly 80% of the increase in persons born elsewhere was due to the increase in numbers of those born in the Irish Republic and enumerated in Great Britain. Of the married women under the age of 50 on census day 21.5% were childless, 30.2% had one child, and only about 10% had four or more children. A comparison with the returns for 1911 shows that the percentage of married women under 45 with five or more children was 21.9 compared with 4.4 in 1951. The average family size for the whole country is now 1.72. Compared with 1911 the average family size of social class 1 has fallen by 30% and by 40 to 45% in the other four social classes. Almost 2½m. persons were enumerated outside private households. Persons in hotels and boarding houses, 840,000, formed the largest group. The next largest groups were: defence establishments, 500,000; civilian hospitals and nursing-homes, 380,000; institutions for mentally ill or deficient, 220,000.

The Population of Glasgow

The Census returns for the City of Glasgow, Volume 1, Part 2, show that the population of the City of Glasgow, 1,089,767, was very slightly smaller, by 3,570 persons, in 1951 than in 1931, a decrease of 0.3%. Although the population has varied little in size there has been a considerable change in its geographical distribution and in its constitution. Large numbers of people have left the older central areas for the outer newer areas. The migration has been mainly to the south; the population of south side wards was 33,000 more in 1951 than in 1931, while the north side wards had 36,570 fewer people than 20 years ago. The section of the city containing the wards of Craigton, Pollokshields, Camphill, and Pollokshaws had an increase of 73,035 persons during the intercensal period. The present population is much older than that of 20 years ago. The percentage of the population in 1931 under 15 years of age was 27.3 and 5.6 at ages 65 and over, compared with 24.8 and 8.6 in 1951. The sex ratio has increased a little, the females exceeded the males by 52,025 in 1951 compared with 39,513 in 1931. The proportion of the population married is larger than formerly, 43.6% in 1951 compared with 36.7% in 1931. During the past 20 years the number of occupied private houses in the city has increased by 37,529—that is, by 14.6%—to a total of 294,467. 24.6% of the persons living in private households were living more than two to a room in 1951. Comparable figures for 1931 are not available, but an estimate places it at 42.3%. Five of the city wards, Hutchesontown, Dalmarnoch, Mile-End, Cowcaddens, and Gorbals, have more than 40% of their population living more than two to a room. 43.9% of the households in the city of Glasgow have the exclusive use of the five amenities listed in the Census schedule—that is, a piped water supply, a kitchen sink, a cooking stove or range, a water closet, and a fixed bath. Half of the households have neither the exclusive use nor a shared use of a fixed bath. About one in 40 of the households has neither a cooking stove nor a range.

Infectious Diseases

Infectious diseases were more prevalent in England and Wales during the week ending October 25 than in the preceding week. The notifications of measles increased by 1,393, from 7,785 to 9,178; scarlet fever by 234, from 1,760 to 1,994; whooping-cough by 132, from 1,074 to 1,206; and dysentery by 55, from 181 to 236.

For the fourth consecutive week the number of notifications of measles has risen by over 1,000. During the week the largest rises in the incidence of measles were Lancashire 265, from 841 to 1,106; Middlesex 219, from 290 to 509; London 130, from 964 to 1,094; and Glamorganshire 110, from 370 to 480. The increase in the incidence of scarlet fever was mainly confined to the Midlands. In the combined area of the north-west counties, Yorkshire, and the northern counties, 615 cases of scarlet fever were notified, 11 fewer than in the preceding week. The largest rise in scarlet fever was 59 in Middlesex, where the cases rose from 93 to 152. The usual oscillations were recorded in the local returns of whooping-cough and no large fluctuations occurred. 28 cases of diphtheria were notified, one fewer than in the preceding week. Half of the total cases were notified in three counties, Lancashire 9 (Liverpool C.B. 4, Huyton-with-Roby U.D. 3); Warwickshire 5 (Birmingham C.B. 5); Glamorganshire (Merthyr Tydfil C.B. 3).

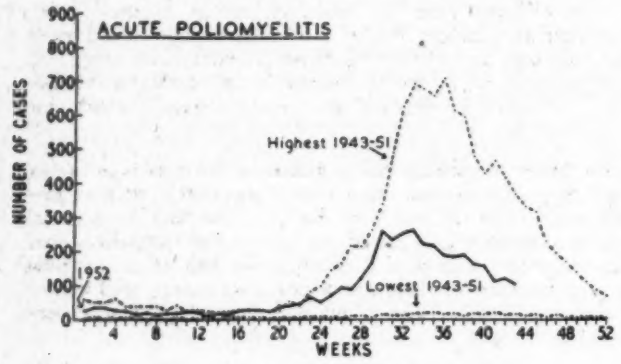
The number of notifications of paratyphoid fever, 8, was 7 less than in the preceding week. Only one case of paratyphoid fever was notified in Wales, where the disease has been prevalent in the preceding 23 weeks. The 8 cases of paratyphoid fever and the 8 cases of typhoid fever were scattered through 11 counties.

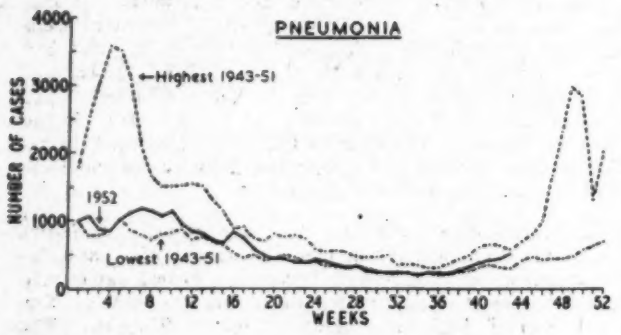
The notifications of acute poliomyelitis numbered 101, and were 11 fewer for paralytic and 7 fewer for non-paralytic than in the preceding week. Thirty-six counties returned a case of acute poliomyelitis compared with 34 in the preceding week. The only county with more than six cases was Essex, where 12 cases were notified from nine areas.

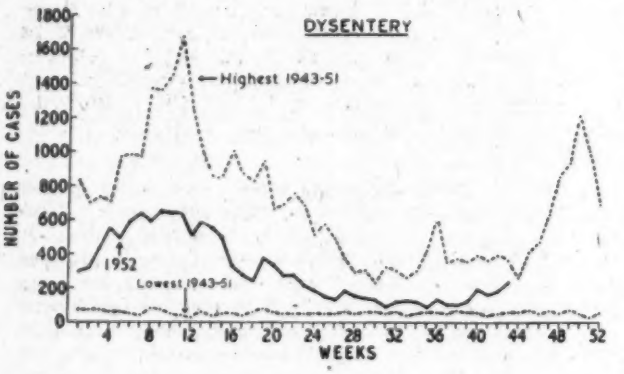
The rise in the incidence of dysentery was contributed by Lancashire with an increase of 60, from 61 to 121. The chief outbreaks in this county were Blackpool C.B. 94 and Liverpool C.B. 9. The only other large returns were Yorkshire West Riding 14, London 13, and Southampton 13.

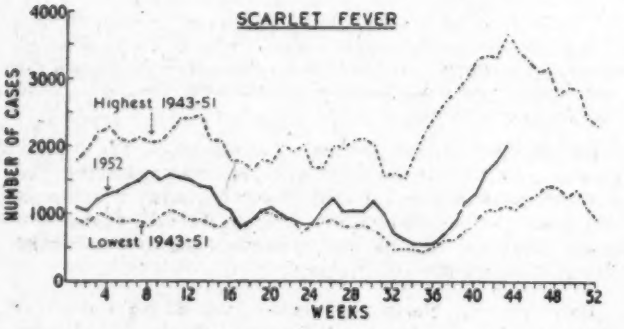
Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the nine years 1943–51 are shown thus - - - - - - -, the figures for 1952 thus ———. Except for the curves showing notifications in 1952, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.









Week Ending November 1

The notifications of infectious diseases in England and Wales during the week included scarlet fever 2,094, whooping-cough 1,449, diphtheria 29, measles 11,223, acute poliomyelitis 86, dysentery 413, paratyphoid fever 7, and typhoid fever 8.

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **October 25** (No. 43) and corresponding week 1951.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the 160 great towns in England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES in Countries and London	1952 Eng. & Wales	1952 Lond.	1952 Scot.	1952 N. Ire.	1952 Eire	1951 Eng. & Wales	1951 Lond.	1951 Scot.	1951 N. Ire.	1951 Eire
Diphtheria	28	1	8	0	2	35	5	13	0	3
Dysentery	236	13	83	2	1	151	47	69	0	
Encephalitis, acute	3	1	0	0		5	0	1	0	1
Enteric fever:										
Typhoid	8	0	0	0		4	1	0	1	0
Paratyphoid	8	0	2 (B)	0		29	1	0	0	1 (B)
Food-poisoning	64	9		0		91	15		0	
Infective enteritis or diarrhoea under 2 years				21	34				16	35
Measles*	9,178	1094	139	42	123	1,962	53	68	110	149
Meningococcal infection	21	1	19	1	2	35	5	18	2	2
Ophthalmia neonatorum	29	3	9	0		30	2	8	1	
Pneumonia†	519	46	251	8	3	419	35	125	2	
Poliomyelitis, acute:										
Paralytic	75	3	} 5	1	4	{ 62	1	} 19	6	3
Non-paralytic	26	1				{ 34	4			
Puerperal fever§	251	22	11	1		207	25	13	1	
Scarlet fever	1,994	200	360	27	103	1,116	97	234	22	38
Tuberculosis:										
Respiratory			135	35				137	38	
Non-respiratory			25	4				22	10	
Whooping-cough	1,206	77	106	26	65	1,441	48	352	45	97

DEATHS in Great Towns	1952 Eng. & Wales	1952 Lond.	1952 Scot.	1952 N. Ire.	1952 Eire	1951 Eng. & Wales	1951 Lond.	1951 Scot.	1951 N. Ire.	1951 Eire
Diphtheria	0	0		0	0	*2*	0	*0*	0	0
Dysentery	0	0		0			0		0	
Encephalitis, acute		0			0		0			0
Enteric fever	0	0		0		*0*	0	*0*	0	
Infective enteritis or diarrhoea under 2 years	9	1	1	0	1	*5*		*3*	2	3
Influenza	10	2	3	0	1	*12*	3	*1*	0	0
Measles		0		0	0		0	*0*	0	0
Meningococcal infection		1					0	*1*		
Pneumonia	205	36		4	4	*173*	33		3	
Poliomyelitis, acute	4	0			0	*6*	0			0
Scarlet fever		0		0	0		0	*0*	0	0
Tuberculosis:										
Respiratory	} 97	{ 10	18	0	5	} *155*	{ 24	*23*	4	7
Non-respiratory		3	3	0	3		3	*4*	0	3
Whooping-cough	2	0		0	0	*3*	0	*0*	0	0
Deaths 0–1 year	233	29	30	6	16	*208*	41	*27*	10	13
Deaths (excluding stillbirths)	5,154	770	540	118	171	*4,708*	780	*566*	121	154
LIVE BIRTHS	7,061	1056	838	209	396	*6,130*	1010	*764*	177	337
STILLBIRTHS	208	32	24			*177*	22	*20*		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia

Medical News

Influenza Vaccine Trials.—The Medical Research Council and Ministry of Health are organizing trials of influenza vaccines this winter. The trials are due to start early in December. About 15,000 volunteers—from industry, hospital nursing staffs, university students, and similar groups—will be inoculated with one of two different vaccines, both of which are made in this country. The intention is to give protection against virus A influenza, the type usually responsible for the severe and widespread epidemics which cause so much loss of time in industry. One vaccine has been chosen by the Medical Research Council's committee on influenza vaccines after encouraging pilot trials last year; the other, regarded as the control, is similar to vaccines which have been available for a number of years. Health records will be kept for the three months following inoculation.

Australian Faculty of Anaesthetists.—Negotiations between the Australian Society of Anaesthetists and the Royal Australasian College of Surgeons have culminated in the establishment of a Faculty of Anaesthetists within the College. The object of the Faculty is "to improve, by all means possible, the art and science of anaesthetics." Sir Gordon Gordon-Taylor attended the inaugural meeting in Melbourne, at which invitations to join the Faculty were given to 40 Foundation Fellows and 62 Foundation Members, and delivered an illuminated message from the Faculty of Anaesthetists of the Royal College of Surgeons of England. Membership of the New Faculty is open to suitably qualified anaesthetists who are approved by the Board of the Faculty; accession to the Fellowship will be by election.

Royal Society Medallists.—Four of the recently announced awards of Royal Society medals are for work to do with medicine. Sir Rickard Christophers receives the Buchanan Medal for his research on malaria and on the anopheline mosquitoes which transmit the disease; Professor J. B. S. Haldane the Darwin Medal for initiating the modern study of the evolution of living populations; Professor Alexander Robertson the Davy Medal for his chemical research, particularly on the glycosides; and Professor F. Zernike, a distinguished Dutch physicist, the Rumford Medal for his work on the development of phase-contrast microscopy.

Kwashiorkor.—An example of the closer links now being established between United Kingdom universities and research institutions and those in Colonial territories is Professor J. S. Heller's visit to Uganda. He recently left the Department of Pharmacology at Bristol for Kampala, where he will study kwashiorkor and oedema in African children in collaboration with the medical faculty of Makerere College and the staff of the Mulago Hospital. Professor Heller has taken with him a graduate assistant and a senior laboratory technician. He is particularly interested in the inter-relation between malnutrition, liver impairment, and water retention, a subject on which he is an authority. Professor Heller's visit will last three months, and is sponsored jointly by the Medical Research Council and the Colonial Office.

Scientific Research in British Universities (1951–2).—A volume summarizing the research projects being undertaken in the scientific departments of British universities has recently been issued by the Department for Scientific and Industrial Research. Details of the research work, which includes research in all branches of medicine, are arranged under each university, and the names of research workers and sufficient information to show the scope of each project are given. An index of names makes it possible to find out where a particular person is working and what he is doing. Each year it is hoped to publish a new edition of the list. Earlier editions were prepared by the British Council for its own use, but, although the council will continue to collect material for future editions, the D.S.I.R. will now be responsible for publication. The present volume (485 pp.) is available from H.M. Stationery Office, price 8s. 6d. net.

The Scientific Exhibition.—Applications for stands at the scientific exhibition to be held at the Annual Meeting (see *Journal*, October 18, pp. 874 and 879) are now being received. Those intending to exhibit are urged to apply without delay, as applications are considered strictly in the order of their receipt. The last day for lodging application forms, which may be obtained from the Secretary, B.M.A. House, Tavistock Square, London, W.C.1, is December 31. It is hoped that, as well as individuals, those in charge of hospitals, medical societies, research institutions, and similar establishments will join in making next year's scientific exhibition a success.

Cortisone Manufactured in Britain.—The first supplies of cortisone acetate manufactured in this country have now been delivered to the Ministry of Health. The starting material was a steroid derived from ox bile. The manufacturers, Bayer Products, Ltd., of London, hope that by the middle of next year their production of cortisone acetate will exceed the present British usage of this material and allow an export surplus.

Regional Hospitals' Consultants' and Specialists' Association.—The annual dinner of the council of the association was held at the Royal College of Surgeons of England last month, with Mr. R. E. Jowett, president of the association, in the chair. The guests were Sir John Charles, Chief Medical Officer of the Ministry of Health, Mr. Rufus Thomas, President of the Association of Whole-time Salaried Specialists, and Mr. P. H. Constable, Principal of the Hospital Administrative Staff College.

Circulation Research.—The American Heart Association has announced the forthcoming appearance of a new bimonthly journal, *Circulation Research*, devoted exclusively to basic studies related to the heart and circulation. The editor-in-chief will be Professor Carl J. Wiggers. The journal will be similar in format to *Circulation*, also sponsored by the association. Annual subscription will be $8.50 (£3 1s.), with a special rate of $6 (£2 3s.) for full-time research fellows. Combined subscription with *Circulation* is offered at the reduced rate of $21 (£7 10s.). The publishers are Messrs. Grune and Stratton, 381, Fourth Avenue, New York, 16.

Christmas Seals for decorating letters and parcels are once again being offered for sale by the National Association for the Prevention of Tuberculosis at a cost of 4s. per hundred. The Association is also selling Christmas cards (6s. per dozen including envelopes). Supplies of both may be obtained through the N.A.P.T., Tavistock House North, Tavistock Square, London, W.C.1. All proceeds from sales will be devoted to the work of the Association.

Emergency Bed Service: Applications and Admissions.—During the seven days ending November 10 the number of applications made by doctors to the London Emergency Bed Service for admission of patients was 947, of whom 92.3% were admitted.

Mr. Andrew Allison, formerly professor of medical jurisprudence at St. Mungo's College, has been elected president of the Royal Faculty of Physicians and Surgeons of Glasgow in succession to Mr. Walter W. Galbraith. For many years Mr. Allison has represented the Royal Faculty on the General Medical Council.

Dr. Andrew B. Semple has been appointed medical officer of health for the City and Port of Liverpool. He was previously the deputy M.O.H. there, and is also lecturer in public health administration at Liverpool University. It will be recalled that Liverpool was the first place in Great Britain to have a medical officer of health, Dr. William Henry Duncan being appointed in 1847.

Dr. Betty Wilmot, a leading Australian maternity and child welfare expert, has joined the staff of the World Health Organization as adviser to the Western Pacific Region. Her parish includes the Philippines, Formosa, Borneo, Indonesia, New Guinea, Australia, and New Zealand. Her main work will be in the Pacific islands, where maternal and child welfare is very backward.

Dr. S. Leonard Simpson is in South America, where he is acting as visiting professor in the faculty of medicine of Buenos Aires University. He is lecturing there on pituitary and adrenal endocrinopathies, and will give other lectures at Rio de Janeiro, Montevideo, Lima, and Santiago.

Mrs. Garnett Passe, widow of the late Mr. E. R. Garnett Passe, the aural surgeon, has left for Boston to read a paper by her husband before the New England Otolaryngological Society next week. The paper is on "Surgery of the Sympathetic for Ménière's Disease, Tinnitus, and Nerve Deafness."

Dr. J. H. Sheldon, senior physician of the Royal Hospital, Wolverhampton, has been elected president of the West Midlands Physicians Association for the 1952–3 session.

Mr. R. R. Simpson, a Hull E.N.T. surgeon, has been appointed next year's president of the North of England Otolaryngological Society.

COMING EVENTS

Radiologists' Postgraduate Course.—The Faculty of Radiologists has arranged a postgraduate week-end course to be held at the Royal College of Surgeons, London, W.C.2, on November 22 and 23, 1952. The fee for the course is 12s. 6d., and further details can be obtained from the Hon. Secretary, Faculty of Radiologists, 45, Lincoln's Inn Fields, London, W.C.2.

United Hospitals Festival Choir.—The choir is giving a performance of Haydn's "Creation" at the Central Hall, Westminster, on November 27 in aid of four national children's charities. Tickets (7s. 6d., 5s. 6d., and 3s. 6d.) are obtainable from Central Hall box office and usual agents; by post from G. J. Piller, 92, Shakespeare Road, Hanwell, W.7.

SOCIETIES AND LECTURES

Details in this column are necessarily brief. Further information and tickets where required (marked ●) should be obtained from the institution concerned

Monday, November 17

HUNTERIAN SOCIETY.—At Apothecaries' Hall, 8.30 p.m., discussion—proposed by Dr. Ff. Roberts and Mr. P. R. Calder and opposed by Mr. J. Griffiths, M.P., and Professor L. P. Garrod: That the Continued Advance in Medicine will Produce more Problems than it Solves.

●INSTITUTE OF CHILD HEALTH.—5.30 p.m., Mr. S. L. Hignett: Pre-natal Mortality in Domestic Animals.

Tuesday, November 18

BRITISH POSTGRADUATE MEDICAL FEDERATION.—At London School of Hygiene and Tropical Medicine, 5.30 p.m., Professor F. J. W. Roughton, Ph.D., F.R.S.: Kinetics of Rapid Chemical and Biological Reactions.

EUGENICS SOCIETY.—At Burlington House, Piccadilly, W., 5.30 p.m., Dr. K. Hutton, D.Phil.: Intelligence Quotients and Differential Fertility.

●INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. D. O'Neill: Psychiatric Aspect of Skin Disorders.

MANCHESTER MEDICAL SOCIETY.—4.30 p.m., Professor H. E. Sigerist: The World of Hippocrates.

SOUTH-WEST LONDON MEDICAL SOCIETY.—At Bolingbroke Hospital, 8.30 p.m., Dr. R. Ewing Rodgers: Coronary Disease.

WEST END HOSPITAL FOR NERVOUS DISEASES.—5.30 p.m., Dr. T. Rowland Hill: neurological demonstration.

Wednesday, November 19

●INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. I. W. Whimster: Reticuloses.

●INSTITUTE OF OBSTETRICS AND GYNAECOLOGY.—At Hammersmith Hospital, 2 p.m., Mr. J. Howkins: Surgery of Carcinoma of the Cervix; 3 p.m., Dr. L. Walter: Radiotherapy of Pelvic Disorders.

●LONDON MARRIAGE GUIDANCE COUNCIL, 78, Duke Street, Grosvenor Square, W.—6.30 p.m., Dr. Ethel Dukes: Frigidity in Married Women.

MIDLAND MEDICAL SOCIETY.—At General Hospital, Birmingham, 8.15 p.m., clinical meeting.

ROYAL EYE HOSPITAL.—5.30 p.m., Mr. L. H. Savin: Surgery of the Ocular Muscles.

ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE.—3.30 p.m., Dr. Wilfrid P. H. Sheldon: Children in Wartime.

ROYAL MICROSCOPICAL SOCIETY.—5.30 p.m., Dr. V. E. Cosslett: *X*-ray Microscopy.

Thursday, November 20

BRITISH INSTITUTE OF RADIOLOGY.—8 p.m., Dr. D. A. G. Galton and Dr. Elspeth M. Ledlie: Chronic Myeloid Leukaemia.

BRITISH POSTGRADUATE MEDICAL FEDERATION.—At London School of Hygiene and Tropical Medicine, 5.30 p.m., Professor R. H. S. Thompson: Cholinesterases and Anti-cholinesterases.

●CHARTERHOUSE RHEUMATISM CLINIC.—5 p.m., Gilbert Scott Memorial Lecture by Sir Adolphe Abrahams: Simplicity and Profundity of Rheumatism.

EDINBURGH CLINICAL CLUB.—At B.M.A. Scottish House, 8 p.m., Dr. D. M. F. Batty: Use of the Antibiotics.

GLASGOW UNIVERSITY MEDICO-CHIRURGICAL SOCIETY.—At Glasgow University Union, 7.30 p.m., Dr. Roberts: Animal Language.

HONYMAN GILLESPIE LECTURE.—At University New Buildings, Edinburgh, 5 p.m., Dr. D. N. Nicholson: Congenital Hypertrophic Pyloric Stenosis.

RESEARCH DEFENCE SOCIETY.—At Physiology Lecture Theatre, University College, London, 5.30 p.m., 21st Stephen Paget Memorial Lecture by Sir Howard Florey, F.R.S.: Advance of Chemotherapy by Animal Experiment.

ROYAL EYE HOSPITAL.—5.30 p.m., Miss J. M. Dollar: Diagnosis of Diplopia.

ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE.—At Liverpool School of Tropical Medicine, Pembroke Place, 7.30 p.m., demonstrations.

ST. ANDREWS UNIVERSITY.—At Materia Medica Department, Dundee, 5 p.m., Dr. W. N. Pickles: Epidemiology in Country Practice.

ST. GEORGE'S HOSPITAL MEDICAL SCHOOL.—5 p.m., Dr. D. Williams: lecture-demonstration in neurology.

Friday, November 21

BRITISH INSTITUTE OF RADIOLOGY.—5 p.m., meeting of medical members.

FACULTY OF RADIOLOGISTS.—At Royal College of Surgeons of England, 4 p.m., Dr. D. M. T. Cones: The Use of Co^{60} in the Treatment of Carcinoma of the Bladder; Dr. John D. Abbatt: Experience in the Diagnosis and Treatment of Polycythaemia Vera During the Use of P^{32}; Dr. Simon Kramer: Treatment of Gliomata with 24 MeV *X*-rays.

●INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. F. R. Bettley: Atopy.

INSTITUTE OF LARYNGOLOGY AND OTOLOGY.—4.30 p.m., Mr. I. Simson Hall: Cancer of the Larynx.

LIVERPOOL MEDICAL INSTITUTION.—8 p.m., Brigadier J. S. K. Boyd and Dr. T. Parker: Epidemiology of Salmonella Typhi-murium Infection.

LONDON UNIVERSITY.—At London School of Hygiene and Tropical Medicine, 5.30 p.m., Professor J. Gough: Pneumoconiosis the World Over.

OSLER CLUB OF LONDON.—At 11, Chandos Street, W., 7.45 p.m., Professor H. E. Sigerist: Medical History in Medical Education.

ROYAL EYE HOSPITAL.—4.30 p.m., Mr. A. J. Cameron: Medical Ophthalmology.

ROYAL MEDICAL SOCIETY, Edinburgh.—8 p.m., Professor R. W. Johnstone: This Hall of Memories (Centenary Address).

APPOINTMENTS

GARDNER, LIONEL DALRYMPLE, M.B., Ch.B., F.R.F.P.S., D.P.M., Medical Superintendent, Ballamona Hospital, Douglas, Isle of Man.

HUTCHISON, ALEXANDER, M.D., Ph.D., F.R.F.P.S., D.P.H., D.P.A., Medical Officer of Health and School Medical Officer, City of Kingston-upon-Hull, and Port Medical Officer of Health and Medical Inspector of Aliens, Hull and Goole Port Health Authority.

NATIONAL HOSPITALS FOR NERVOUS DISEASES, Queen Square, London, W.C.—*Assistant to the Department of Psychological Medicine at the National Hospital, Queen Square, W.C.*, R. F. T. Grace, M.D., M.R.C.P. *Anaesthetists to the Maida Vale Hospital for Nervous Diseases, W.*, T. B. L. Roberts, M.R.C.S., L.R.C.P., D.A., and N. C. B. Trapps, M.R.C.S., L.R.C.P., D.A.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Goldman.—On October 29, 1952, at Sunderland Maternity Hospital, to Dr. and Mrs. Henry F. Goldman, a son—Trevor Rodger.

Nohl.—On November 2, 1952, at the Memorial Hospital, Woolwich, London, S.E., to Inge, wife of Mr. H. C. Nohl, F.R.C.S., a son.

Tepper.—On November 8, 1952, at Bromley Maternity Hospital, Kent, to Rachel (formerly Claiman), wife of Dr. R. Tepper, M.R.C.P., a daughter.

Wilkie.—On August 10, 1952, at the Jessop Hospital, Sheffield, to Noreen (formerly Keer), wife of Dr. D. J. K. Wilkie, a daughter—Helen Katharine.

DEATHS

Ainley.—On October 24, 1952, at Harrogate, Frederick Shaw Ainley, M.B., C.M., of "Oakfield," Wheatlands Road, Harrogate, formerly of Stainland, Yorks, aged 81.

Bayon.—On October 20, 1952, at Little Shelford, Cambridge, Henry Peter George Bayon, M.D., Ph.D.

Connell.—On October 31, 1952, in an infirmary, Glasgow, William Kerr Connell, M.B., F.R.C.S., F.R.F.P.S.Glas., D.T.M.&H., of 2, Wellshot Drive, Cambuslang, Glasgow, aged 58.

Dunn.—On October 21, 1952, at 16, Lansdown Crescent, Bath, Henry Nason Dunn, C.M.G., D.S.O., M.B., B.Ch., Colonel, late R.A.M.C., retired, aged 88.

Johnson.—On October 30, 1952, William Crosby Johnson, M.B., Ch.B., of Mayfield Lodge, Haslemere, Surrey, late of Manchester and St. Andrews, aged 77.

Malone.—On October 22, 1952, at Mid-Herts Hospital, St. Albans, William Aloysius Malone, L.R.C.P.&S.I. & L.M., late Colonial Medical Service.

Pentreath.—On October 23, 1952, Herbert Massingherd Pentreath, M.C., M.R.C.S., L.R.C.P., of 62, Walliscote Road, Weston-super-Mare, Som.

Scott.—On October 14, 1952, at his home, Plumstead, Capetown, South Africa, Ralph Lester Scott, M.B., F.R.C.S.Ed.

Sillar.—On October 23, 1952, William Cameron Sillar, M.D., of The Gables, Wheatley, Oxon, aged 88.

Smeed.—On October 25, 1952, Edward Smeed, M.R.C.S., L.R.C.P., of Hendon, London, N.W.

Steen.—On October 19, 1952, at Hammersmith Hospital, London, W., Robert Kenneth Steen, L.R.C.P.&S.Ed., L.R.F.P.S.Glas., aged 28.

Walker.—On October 21, 1952, at Springbank, New North Road, Huddersfield, Edward Walker, M.B.E., M.D., aged 89.

Any Questions?

Correspondents should give their names and addresses (not for publication) and include all relevant details in their questions, which should be typed. We publish here a selection of those questions and answers which seem to be of general interest.

Focal Sepsis

Q.—*Opinion has now swung far away from focal sepsis as a frequent cause of ills elsewhere in the body. Can you please state in what general conditions focal sepsis is still believed to play a significant part? Is it, for instance, an aetiological factor in cholecystitis or hepatitis? Is it always wise to eliminate focal sepsis wherever and whenever found?*

A.—Focal sepsis is no longer considered to be the direct cause of any other disease, though it may make the attack more severe. It is responsible for general ill-health, and if severe the ill-health may be serious. Its effect is best shown in a disease like diabetes mellitus, where glycosuria may reappear and the insulin requirements increase if focal sepsis appears or becomes worse. Removal of the septic focus will, after a while, usually enable the dose of insulin to be reduced. In toxic goitre, septic foci in the tonsils will cause a great increase in the symptoms, pulse rate, and basal metabolic rate, and eradication of the foci will be followed by an improvement. The condition may be so severe, however, that it is safer to deal with the goitre either by thiouracil or by operation before the tonsils are removed. Various other diseases are made worse, but the evidence is not so clear as in these two diseases, where direct measurements are possible. It is impossible to prove that the general ill-health due to focal sepsis lowers the resistance of the body to other diseases and so enables them to develop, but it is an attractive hypothesis. It is considered unwise to permit definite focal sepsis to continue untreated. There is no evidence that it acually causes a cholecystitis or hepatitis.

"Blown" Tins

Q.—*What is the right policy to adopt towards a "blown" tin of food? Does a tropical climate affect the decision on what should be done? I have opened many of these tins and the contents appear perfect, and on several occasions I have eaten from them without ill-effect. If such tins are all destroyed the financial loss is considerable. Is there any test which can be used to decide whether the contents of a blown tin are safe to eat? Alternatively, will any treatment of the contents make them safe?*

A.—A "blown" can results from the production of gas, which converts the normal slight vacuum in a properly processed can into a positive pressure. The gas may be of chemical origin, as when hydrogen is produced by the action of acid fruits on the metal of the can, or of bacterial origin. Many of the bacteria responsible for spoilage belong to the thermophilic group, multiplying best at temperatures of 50 to 60° C. Cans containing these organisms often cause no trouble in cold climates, but become blown when exposed to tropical temperature. As there is no test short of a full bacteriological examination to decide what the cause of blowing is in any particular can, the only administrative decision that can be taken is to condemn the food. The cans, or a proportion of them, should be returned to the manufacturers so that they can make the necessary alterations in processing to prevent recurrence of the trouble. In this they can appeal for help to the British Food Manufacturing Industries Research Association.

Blown cans of food may often be eaten with impunity, but others are dangerous, and there is no simple method of rendering the contents safe. Whatever risks the individual may care to take, batches of blown cans intended for general consumption must be condemned.

Barbiturates and Autonomic Activity

Q.—*What is the action of barbiturates on the autonomic nervous system?*

A.—The barbiturates have a powerful depressant action on the hypothalamic centres controlling autonomic activity. They diminish the motor, sympathetic, and emotional responses resulting from electric stimulation of the hypothalamus in cats, and they selectively depress the brain stem, and therefore the vasomotor and respiratory centres, in doses which do not exert a full effect on the cortex. The evidence that the barbiturates exert a peripheral effect on the autonomic nervous system is less satisfactory. The recorded effects vary with individual members of the group and with the species of animal studied. In general, full anaesthetic doses have to be administered to elicit these effects, which include diminished excitability of the vagus supply to the heart, reversal of the effect of the vagus on the stomach (amylobarbitone), and reversal of the effect of the sympathetic on the stomach (phenobarbitone). The proprioceptive mechanisms (carotid sinus) regulating vasomotor tone are depressed. The laryngeal spasm which may follow intravenous thiopentone is probably due to stimulation of the peripheral vagal endings.

In clinical practice when barbiturates are used in the treatment of psychosomatic disorders it is the effect on the hypothalamus which it is hoped to elicit. There is little evidence of any significant peripheral effect on the gastrointestinal tract or uterus unless the patient is rendered almost unconscious.

Care of Mental Defectives

Q.—*What public provision is made for the institutional care and training of mental defectives? How is admission secured?*

A.—Institutions for mental defectives are hospitals within the meaning of the National Health Service Act and the responsibility for providing them rests with regional hospital boards. For admission it is usually necessary in the first instance to apply to the medical officer of health of the county or county borough in which the patient lives in order that he may be "ascertained" under the Mental Deficiency Act, 1913, and his name sent up to the regional board. But all regional boards have long waiting-lists for vacancies in their hospitals for mental defectives, and only the most urgent cases can be considered. For more detailed information reference should be made to a pamphlet (price 9d.) published by the National Association for Mental Health, 39, Queen Anne Street, W.1, under the title "Notes on Legislation for Mental Defectives."

"De Nol"

Q.—*What are the principles of the "De Nol" treatment for peptic ulcer? Are there any reasons for believing it to be more effective than the standard treatment with diet and alkalis?*

A.—The De Nol treatment for peptic ulcer has been evolved in South Africa. Patients treated by the method are given a full diet and a graduated series of medicines. The medicines are compounded of numerous remedies (for example, liquor bismuthi concentratus, acidum hydrocyanicum dilutum, tinctura belladonnae, etc.) and one component is changed with each change of medicine. In addition the medicines contain an unspecified amount of the "Denolate radicle" which is "synthesized in the laboratory by a process of controlled symbiotic fermentation." The nature of this compound has, so far, not been disclosed. It is claimed that the medicines containing the "denolate radicle" combine with the ulcer surface to form a thick and tenacious mucilaginous cover which protects it against further digestion while healing takes place underneath, and that their ability to do this is partly owing to the fact that they are "subjected to the appropriate degree of electro-static tension." However, we know of no published experimental evidence to support such a remarkable claim.

The makers of De Nol claim excellent therapeutic results from their product. However, a large proportion of peptic-ulcer patients put on any non-injurious regime must be expected to do well, as the natural course of the disease is for remission to occur. In addition, evidence is now becoming available that a full diet is compatible with normal healing. It may even be—though this is not proved—that over-restricted dieting hinders healing in some patients, and a change to a full diet is always worth trying. The expense of the De Nol treatment (about £14 a course) may induce in some patients a mental state receptive to a suggestion that the disease is being cured. There is, however, no reason to suppose that this cannot be done more cheaply and more effectively by standard therapy.

Shot-gun Accident

Q.—*A patient has been peppered by about 40 pellets from a shot-gun. What are the chances of lead poisoning or of a pellet lodging in an end-artery and causing serious complications? What treatment is advised? The pellets are widely scattered in the body.*

A.—The risk of lead poisoning is negligible, and the chance of an end-artery becoming blocked almost equally remote. The only treatment is removal of the pellets where practicable, and *x*-ray examination to help exclude internal injury or suggest possible later complications. There is, of course, always the risk of bacteria being introduced by the pellets, and prophylaxis against tetanus should be considered.

Onset of Aplastic Anaemia after Chloramphenicol

Q.—*If aplastic anaemia is going to develop after treatment with a drug such as chloramphenicol, when will it develop? Does it ever appear after treatment has ceased? If so, when may a patient be regarded as safe from this complication after a course of a predisposing drug?*

A.—The following comments are based on an analysis of about 20 published cases; not enough is known to allow a dogmatic answer.

Aplastic anaemia may occur during or after the completion of a course of chloramphenicol. The commonest sequence is (1) sensitizing course of chloramphenicol; (2) interval of days, weeks, or months; (3) precipitating course of chloramphenicol. Sensitization and precipitation may each require no more than 4 capsules (200 mg.) chloramphenicol. Treatment with chloramphenicol continued for a month or more may produce aplastic anaemia even though dosage is continuous. Aplastic anaemia does occur, though rarely, as a result of a single course of 18–20 capsules of 50 mg. given to a child. If aplastic anaemia does develop, the presenting symptoms are likely to be ready bruising, purpura, lassitude, and spontaneous bleeding; these normally occur within two months of the completion of the course, and even in the most insidious cases lassitude and tiredness become prominent within three months. When anaemia or thrombocytopenia do develop the prognosis is very bad: only one or two cases appear to have recovered.

Fortunately the complication is rare, occurring probably in no more than 1 case in 10,000 treated. On the one hand, therefore, one must not become too alarmed by the risk, but on the other it is essential that chloramphenicol be prescribed only when there is a clear indication for it, and for infections in which no other drug is active, such as typhoid fever. It would probably be wise to prescribe aureomycin for undulant fever rather than chloramphenicol, which has hitherto been the drug of choice. It is difficult to decide how justifiable is its routine use in pertussis; the writer's own view is that it should be used whenever there is a risk of death or serious complication—that is, in all children under the age of 1 year, and in any debilitated child or in one suffering from multiple infections. Its use in otherwise healthy children who are likely to recover without complications may be open to some criticism.

The Ovaries and Breast Cancer

Q.—*Does castration affect the prognosis of cancer of the breast in women? Is there any justification for its use, in conjunction with radical surgery, either routinely or in selected cases of breast cancer?*

A.—The removal of the ovaries in cancer of the breast is never harmful so far as the malignant condition is concerned and is often helpful. If menstruation has not ceased it is a very useful thing to do, and after the climacteric it is still worth while because the ovaries are not completely inert after the change of life. There is evidence to show that suppression of ovarian function by *x*-ray treatment is not so valuable as surgical removal of the ovaries. In two types of case is ovariectomy specially indicated—the hopelessly inoperable and the case of recurrent disease after surgical amputation or radiation.

For some reason or other the practice of removing the ovaries in this condition has never become established here or in any other country, but probably it will become increasingly popular.

High-flying Mosquitoes

Q.—*What effect has altitude on the viability of mosquitoes, with particular reference to their ability to survive in aeroplanes?*

A.—Altitude does not appear to affect the viability of mosquitoes in aeroplanes. In three personally conducted trials the results were as follows: (1) At 15,000 ft. (4,572 m.) in a non-pressurized aircraft 2,000 anopheline mosquitoes were taken from England to North Africa during the war in small cages; at the end of the journey all except five had survived. (2) At 10,000 ft. (3,048 m.) in a non-pressurized aircraft 2,000 anopheline mosquitoes were taken from England to West Africa in 1947. All except three survived the journey. (3) In a chamber evacuated to correspond with a height of 35,000 ft. (10,668 m.) all the mosquitoes survived for one hour.

NOTES AND COMMENTS

Sedatives for Babies.—Dr. T. H. J. WILLIAMS (Eastleigh) writes: I personally have not found chloral hydrate a satisfactory sedative ("Any Questions?" October 18, p. 890). I have found it very difficult to persuade children to take what my daughter calls "burny medicine." The best are tablets of carbromal and bromvaletone or aspirin and calcium carbonate, a quarter to a whole tablet of either. These, of course, can be given with jam.

OUR EXPERT writes: There can, of course, be no doubt that your correspondent is correct in saying that chloral has an unpleasant taste. It certainly has. This can be got over to some extent by careful prescribing:

e.g. Syrup of chloral	10 min. (0.6 ml.)
Liquid extract of liquorice ..	2 min. (0.12 ml.)
Glycerin	10 min. (0.6 ml.)
Water to	60 min. (3.6 ml.)
Send 1 fl. oz. (28.4 ml.)	

In such a mixture each 60 min. (3.6 ml.) contains nearly 2 gr. (0.13 g.) of chloral hydrate. I cannot help feeling, however, that the advantages of chloral as a hypnotic for children greatly outweigh the disadvantage of its disagreeable taste, which is slight when prescribed as above, and that it is more dependable and better tolerated than the urea hypnotics to which your correspondent refers. Chloral and acetylsalicylic acid cannot, of course, be compared. The former is a potent hypnotic, the latter an antipyretic-analgesic.

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